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HEALTH-RELATED QUALITY OF LIFE IN WOMEN WITH BREAST CANCER IN IRAN

A Methodological and Clinical Study

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ABSTRACT

Background: Breast cancer is the most common cancer in women in Iran and is the most common cancer in women both in the developed and the developing world. Living with breast cancer often involves making fundamental changes in life. The breast cancer illness trajectory may negatively affect various dimensions of the patients' health-related quality of life (HRQoL), but may also vary greatly between individuals. The main aim of the present thesis was to investigate HRQoL and its determinants as well as to study coping abilities in women with breast cancer living in Iran in comparison with women without breast cancer before final diagnosis and 6 months later.

Method: The thesis is based on four studies. The first two studies are methodological and include five self-rated psychometric instruments for the Persian language: Health Index (HI), Sense of Coherence (SOC) scale, Spirituality Perspective Scale (SPS), Brief Religious Coping (RCOPE) scale and SF-12 Health Survey version 2 (SF-12v2). The psychometric tests were given to a healthy sample of Iranian population (n=333). In the third study the five instruments were applied at the pre-diagnosis phase (T1) and 6 months later (T2) in a sample of women with breast cancer (n = 162) and in a control group of women seeking mammography who were subsequently diagnosed as not having breast cancer (n= 639). In the fourth study, using the same samples as in Study III (women with breast cancer and controls), the mediating effect of SOC was investigated.

Results: Almost all hypotheses tested for validity were confirmed. An exploratory factor analysis and structural equation modeling for the SF-12v2 verified a two-factor structure (a physical component summary and a mental component summary) in accordance with the original factor structure. The reliability of the instruments as measured by internal consistency and intra-class correlations was satisfying. When compared with the control group, the Iranian women with breast cancer rated impaired physical functioning, fatigue and financial difficulties most prominent during the first 6 months after pre-diagnosis. At the same time, the patients with breast cancer improved their perception of global quality of life and emotional functioning. The most important predictors of the HRQoL dimensions were SOC followed by baseline ratings of the respective dimensions. Furthermore, SOC mediated the role of baseline values of HRQoL to follow-up HRQoL values after 6 months. The concept of SOC was a stronger predictor of HRQoL than religious coping and spirituality.

Conclusion: The SOC, HI, SPS, Brief RCOPE and SF-12v2 were found to be psychometrically sound instruments, implying that they are suitable for use in health surveys in an Iranian population. When planning nursing care for women with breast cancer in Iran, it is important to integrate HRQoL measures early in the illness trajectory. Our findings suggest that focus should be on physical functioning, fatigue and financial difficulties. As in other cultures, the concept of SOC seems to be applicable to the Iranian context and thus should be considered in individual valuation of coping ability along with religious coping and spirituality.

Key words: health-related quality of life, breast cancer, sense of coherence, spirituality, religious coping, well-being, psychometric tests

To my beloved family

in memory of my beloved brother, Kamyar

and my dearest friend Akhtar

LIST OF PUBLICATIONS

I.   Rohani C., Khanjari S., Abedi H-A., Oskouie F., Langius-Eklöf A. Health index, sense of coherence scale, brief religious coping scale, and spiritual perspective scale: psychometric properties *Journal of Advanced Nursing, 2010: 66 (12), 2796-2806.*

II.   Rohani C., Abedi H-A., Langius-Eklöf A. The Iranian SF-12 Health Survey version 2 (SF-12v2): factorial and convergent validity, internal consistency and test-retest in a healthy sample *Iranian Rehabilitation Journal, 2010: 9 (12), 4-14.*

III.   Rohani C., Abedi H-A., Omranipour R., Langius-Eklöf A. Pattern of changes in health-related quality of life, sense of coherence, spirituality and religious coping in a sample of Iranian women with breast cancer: A prospective and comparative study starting before diagnosis *(Manuscript).*

IV.   Rohani C., Abedi H-A., Sundberg K., Langius-Eklöf A. Sense of coherence as a mediator of health-related quality of life dimensions in patients with breast cancer 6 months after diagnosis *(Manuscript).*

CONTENTS

LIST OF ABBREVIATIONS

QoL	Quality of Life
HRQoL	Health-Related Quality of Life
HI	Health Index
SOC	Sense of Coherence
RCOPE	Religious Coping
SPS	Spiritual Perspective Scale
MOHE	Ministry of Health & Medical Education
LISREL	Linear Structural Relationships Analysis
EORTC QLQ-C30	European Organization for Research and Treatment of Cancer
PF	Physical Functioning
RF	Role Functioning
EF	Emotional Functioning
CF	Cognitive Functioning
SF	Social Functioning
FA	Fatigue
NV	Nausea and Vomiting
PA	Pain
DY	Dyspnea
SL	Insomnia
AP	Appetite Loss
CO	Constipation
DI	Diarrhea
FI	Financial Difficulties
EORTC QLQ-BR23	European Organization for Research and Treatment of Cancer
BI	Body Image
SEF	Sexual Functioning
SEE	Sexual Enjoyment
FU	Future Perspective
ST	Systemic Therapy Side Effects
BS	Breast Symptoms
AS	Arm Symptoms
HL	Upset by Hair Loss
SF-12v2	Short Form 12-item Health Survey version 2
PCS	Physical Component Summary
MCS	Mental Component Summary
GH	General Health
RP	Role Physical
RE	Role Emotional
MH	Mental Health
VT	Vitality
CFI	Comparative Fit Index
SRMR	Standardized Root Mean Square Residual
NNFI	Non-Normed Fit Index
IFI	Incremental Fit Index
AIC	Akaike Information Criterion
ECVI	Expected Cross-Validation Index

1 BACKGROUND

1.1 BREAST CANCER AT A GLANCE IN THE WORLD

Breast cancer is ranked second in the world as the most frequent cancer among women (23% of all cancers) with more than one million cases worldwide every year (Globocan, 2008). It is now the most common cancer in high, low and middle-income regions with about 690,000 new cases estimated in each region (population ratio 1:4) (Globocan, 2008). Incidence and mortality rate of breast cancer alter substantially throughout the world. Generally, incidence rate is considered high when it is greater than 80 per 100,000 and low when it is less than 40 per 100,000 (Parkin & Fernandez, 2006). Incidence rate of breast cancer varies from 19.3 per 100,000 women in Eastern Africa to 89.7 per 100,000 women in Western Europe (Globocan, 2008). Breast cancer ranks as the fifth cause of death among cancers in general. Survival rates are now increasing because of a combination of early detection efforts in the forms of mammography screening programs and advancement in treatment regimens (Parkin & Fernandez, 2006). Breast cancer survival rates vary prominently worldwide, ranging from 80% or over in North America, Sweden and Japan to 60% in middle-income countries and less than 40% in low-income countries (Coleman et al., 2008).

Mammography is known to reduce breast cancer mortality by 20% to 30% in women over 50 years old in high-income countries where mammography coverage is over 70% (Boyle & Levin, 2008), but probably < 20% in women aged 40-49 years (Elmore et al., 2005). There is no evidence on the effect of screening through breast self-examination (BSE) (Boyle & Levin, 2008). However, BSE can empower the women to take responsibility for their own health and is recommended for increasing awareness among women at risk rather than as a screening method (Boyle & Levin, 2008).

1.1.1 Breast cancer treatment

Treatment for breast cancer mainly depends on several factors: the cancer stage and the type of breast cancer, such as characteristics of the cancer cells and presence of estrogen receptors in the tumor and also menopausal status, metastasis and the patient's general health status (MD Anderson, 2011). To control the possibility of spreading and to increase survival rates single or combined treatment is normally applied. There are various types of treatment, including surgery, chemotherapy, radiotherapy and hormone therapy, but today the therapy mostly recommended to be targeted to the characteristics of the tumor (Chapman & Moore, 2005). Treatment for operable tumors starts with surgery, which implies removal of the cancer and surrounding breast tissue in the form of conservative surgery or mastectomy depending of regional routines (MD Anderson, 2011). Surgery is followed by radiation therapy or adjuvant systemic therapy (a standard protocol of chemotherapy), with or without hormone therapy (MD Anderson, 2011).

1.2 IRAN: THE CONTEXT OF THIS STUDY

Iran, located in the Middle East, a region between Asia, Europe and Africa, ranks as the 18th largest country in the world with an area of 1, 648,195 km^2 .The country is divided into 31 provinces, which are divided into counties and subdivided into district and sub-districts (Mehrdad, 2009). Iran has a population of about 74.2 million (UNFPA, 2009),

with more than 7.7 million living in the capital Tehran (Hosseini et al., 2010). Iran's population is young, about 69% of the population are urban inhabitants and almost one third is less than 15 years of age (Mehrdad, 2009) (7.3% are aged 60 years or over) (Hosseini et al., 2010). The population annual growth rate between 2005 and 2010 is 1.2% (UNFPA, 2009). Iran is a country with diverse ethnic backgrounds and the majority of the population speaks the Persian language, which is also the official language of the country (Iran Chamber Society, 2011).

1.2.1 Health care system in Iran

Iran's health care system has gone through many major changes over the past two decades. Primary health care (PHC) centers were implemented both in the rural and urban areas in 1984 and public health services provided through a Nationwide Health Network (Asadi-Lari et al., 2004). The private sector plays a significant role in health care provision in Iran, where it mainly focuses on medical and rehabilitation services in urban areas. The Ministry of Health and Medical Education (MOHE) mandates planning and the monitoring of health-related activities in the public and private sectors, in addition to the education of medical groups, including physicians, nurses, physiotherapists, and so on (Mehrdad, 2009). In 2008, approximately 90,000 nurses and 80,000 physicians were working in Iran's heath care system both private and governmental (Zarea et al., 2009).

There is a National Cancer Registration (pathologic-based center report) in Iran and the pathology laboratory in each hospital responsible for registering and reporting the information of the patients to the MOHE (Mousavi et. al, 2009). Within a Nationwide Health Network, in rural areas general practitioners refer the patients with cancer or suspected cancer to the university hospitals located in urban areas. In urban areas cancer services are principally organized through the Medical Universities or private hospitals in the form of multidisciplinary teams. The patients with a lump in the breast or a suspect symptom meet a wide range of services of specialists and other professionals for biopsy, surgery, rehabilitation and adjuvant treatments (Moradian, Aledavood, & Tabatabaee, 2011).

A comprehensive national cancer control program (CNCCP) was designed and approved by the Nutrition and Health Group of the Academy of Medical Sciences of the Islamic Republic of Iran in early 2007 (Mousavi et al. 2008a). The plan included multi-dimensional approaches to cancer, including prevention, early diagnosis, effective treatment and palliative care programs, which are all an integral part of preventing cancer and providing an appropriate care for cancer patients (Mousavi et al., 2008a).

1.2.2 Health system financing

Iran is an upper middle-income country spending 6.3% of its gross domestic product (GDP) on health (UNFPA, 2009). Iran has increased investment in health during the past 10 years. Despite, government support on health costs out-of-pocket expenditure on health remains as high as 55% (Mehrdad, 2009). Health care is commonly financed through a combination of public payment, consumer co-payments and income (Moradian, Aledavood, & Tabatabaee, 2011). Health services are divided between PHC fully financed by the government and medical benefit packages financed through health insurance (Moradian, Aledavood, & Tabatabaee, 2011). According to official data,

more than 90% of the Iranian inhabitants are under the coverage of at least one kind of health insurance (Mehrdad, 2009). However, in most cases patients confront a co-payment at the point of getting services (Moradian, Aledavood, & Tabatabaee, 2011). A small percentage of Iranian people are not covered by any of the health insurance organizations (Ibrahimpour et al., 2011).

1.2.3 Breast cancer in Iran

Breast cancer is the most common cancer in Iranian women with the first rank among malignancies in women, comprising 24.4% of all neoplasms (Mousavi et al., 2009) and with an age-standardized rate (ASR) of 25.1 per 100,000 female inhabitants in 2006 (Mousavi et al., 2010). There is an increasing trend with a peak from the ages 40 to 49 years (Mousavi et al., 2007). Interestingly, wide variations in the incidence of breast cancer have been shown within the country, with higher incidence rates in the areas of South and Central Iran (Mousavi et al., 2010).

The findings of a study by Mousavi et al., (2010) indicated that the risk of breast cancer among Iranian immigrants (residing in Sweden for 16 years) was higher (ASR: 58.3 per 100,000 female inhabitants) than Iranian residents (ASR: 25.1 per 100,000 female inhabitants), but lower than for the native Swedish population (ASR: 79.9 per 100,000 female inhabitants). The reasons for the decreased risk for cancers among the Iranian immigrants were suggested to relate to differences between the registry systems, selected immigrant groups and environmental exposures (Mousavi et al., 2010).

Early detection of breast cancer remains an important challenge. At the national level in Iran, mammography screening of breast cancer is still not routinely prescribed. However, programs teaching women how to perform breast self-care examinations and when and why to ask for breast examination is now available in rural and urban health centers (Harirchi et al., 2010). Even if it was possible to afford mammography screening for women aged 50-69 years in Iran, there would still remain the necessity of early detection of breast cancer for women aged 35-49 years (peak age at 40-49). Given the importance of premature mortality from breast cancer, especially in women under the age of 50 years in Iran, there is a need to establish whether simpler approaches than mammography could provide some benefit in a country where the majority of breast cancers are diagnosed at an advanced stage (Mousavi et al., 2008b).

1.3 THE CONCEPT OF HEALTH-RELATED QUALITY OF LIFE

Over the past 30 years, the concept of quality of life (QoL) has been proposed as an important outcome for the evaluation of health care in cancer (
King & Hinds, 2003; Ferrans, 2005). QoL is considered a key component in nursing (King, 2006). Nursing is a caring practice, and as a scientific discipline, it is naturally involved in the assessment, measurement and promotion of QoL in patients with cancer (Grant & Dean, 2003). The philosophy of a holistic approach in nursing is consistent with focusing on QoL (King et al., 2002). Even though the concept of QoL is recognized as one important area to consider in the care of individuals with illnesses, it is difficult to define because of its meaning in different contexts by different persons (Fayers & Machine, 2007). The World Health Organization Quality of Life (WHOQOL) Group has defined QoL as "individuals perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns" (WHO, 1997). WHO defines

Health-Related Quality of Life (HRQoL) as a subjective, multidimensional and dynamic concept of physical, mental and social functioning in relation to a medical condition (WHO, 1997).

The concepts of QoL, HRQoL and well-being, are sometimes used interchangeably and the lack of a distinction in definition of the constructs might leads to conceptual and operational confusion (Patrick, 2003). The concept of well-being is a subjective and positive construct, a positive state more than absence of physical and psychological problems that includes physical, emotional and social dimensions and is defined as an individual's cognitive and affective evaluation of life (Bowling, 2005). The term HRQoL is generally used to define aspects of life affected by illness and treatment (e.g., physical and mental functioning, symptoms, treatment toxicities, work and role responsibilities, social and family life and spiritual concerns) (Patrick, 2003; Ferrans, 2005; Fayers & Machine, 2007). There is no universal accepted definition of HRQoL and it is still under debate today (Fayers & Machine, 2007), but there is consensus about its being subjective, contextual and multidimensional (King, 2002; Bowling, 2005; Plummer & Molzahn, 2009). HRQoL usually includes self-report measures of physical and mental health, as well as spiritual, environmental and social aspects (Cella, 1994; Bowling 2005; Bahrami 2011). During the past decades, several standardized questionnaires have been developed to measure HRQoL (Bowling, 2005; Haberman & Bush, 2003; Fayers & Machine, 2007). Today, a clinical trial includes a measure of HRQoL, to predict survival rates, document patterns of impairment and complete recovery, compare the results of different types of treatment, and establish norms of morbidity among diverse cultural groups and population of cancer survivors (Haberman & Bush, 2003, p 174). HRQoL from a nursing perspective is an important outcome variable and can be of guidance in prognosis, treatment, symptom management, monitoring, clinical decision-making, and supportive nursing care interventions (Goodwin et al., 2003; Perry, Kowalski & Chang, 2007; Quinten et al., 2009).

To cover different aspects of HRQoL, the use of multiple instruments is required (Fayers & Machine, 2007). Generic instruments should be supplemented with disease and symptom targeted instruments to provide complementary information (Fayers & Machine, 2007). Furthermore, HRQoL instruments should be valid and reliable in each culture in which they are studied (Cella et al., 2002; Fayers & Machine, 2007).

In this thesis, HRQoL has been operationalized as the women's subjective evaluation based on the individual's perception on health and aspects of life affected by illness and treatment (e.g., physical and mental functioning, symptoms, treatment toxicities, work and role responsibilities, social and family life and spiritual concerns) (Padilla, 2003).

1.4 LIVING WITH BREAST CANCER

Cancer occurs in an unpredictable course from diagnosis to treatment, cure and death. Living with cancer often involves changes in the life of the breast cancer patient (Wells, 2008). Overall, when the experience of women shows that there is something wrong in the breast, they may perceive uncertainty and high anxiety during the diagnostic period (Liao et al., 2008). This experience continues throughout the diagnosis and treatment process (Wells, 2008). As a stressful experience, breast cancer negatively might affect various dimensions of the patients' HRQoL (Fayers & Hays 2005; King, 2006). Women with breast cancer may perceive fatigue, physical and psychological symptoms

along with specific side effects of treatments (Brandberg et al., 2003; Montazeri et al., 2008). The results of an extensive qualitative study on overall impact of breast cancer between 1 to 5 years since diagnosis within various ethnic groups indicated that Asian-American women were the only ethnic groups that reported decreased long-term HRQoL (Ashing-Giwa et al., 2004). Furthermore, the results of another qualitative study on perspectives of cancer patients in Iran revealed that they probably suffer more from the impact of cancer on their daily life rather than symptoms related to disease and treatment. The cancer diagnosis itself affected daily life, which included financial disruption, inability to work and to manage family life indicating a need for holistic care (Moradian, Aledavood, & Tabatabaee, 2011).

Patients with cancer in Iran described their experiences in a phenomenological study as life full of suffering and a continuous struggle, where chemotherapy was the most difficult experience (Nasrabadi et al., 2011). A review of the literature on measures of HRQoL in women with breast cancer revealed conflicting results (Härtl et al., 2010a). Several studies reported significant improvements in most HRQoL dimensions within 6 months after diagnosis (Arora et al., 2001; Lu et al., 2009; Eisenbraun et al., 2011). Although some problems (e.g., anxiety, body image impairments and sexual functioning) may still remain (Härtl et al., 2010a), a clear reduction is observed for breast and arm symptoms (Salonen et al., 2010). However, some studies show that side effects increase within the first 6 months after treatment along with either stable (Schou et al., 2005) or worse overall HRQoL (Lu et al., 2007; Hatam et al., 2011).

Follow-up studies up to 12-24 months after diagnosis have also presented conflicting results. Some studies indicate that patients experience HRQoL impairments, poor self-perceived health and problems with psychosocial adjustment (Ganz et al., 2003; Arndt et al., 2005; Lee et al., 2011), whereas others show unaffected or even improved HRQoL after treatment (Ganz et al., 2002; Schou et al. 2005; Härtl et al., 2010b). One reason for the contradictory results could be the time when the measurements are performed. The baseline is most often at the time of diagnosis (Schou et al., 2005; Lee et al., 2011) or the post-diagnosis period (Shimozuma et al., 1999; Budischewski et al., 2008; Härtl et al., 2010b). These data provide a point of comparison for the remaining measurements, which can influence the interpretation of the results. The most meaningful time point of comparison is before the diagnosis of cancer (Haberman & Bush, 2003), but a baseline measurement before diagnosis is not easy to obtain. It seems that there is an overall lack of longitudinal studies with a baseline before diagnosis and therefore there are difficulties to make general inferences regarding how HRQoL is affected during the disease trajectory of a breast cancer diagnosis (Härtl et al., 2010a).

A high number of locally published HRQoL studies in women with breast cancer in Iran are available, but the number of internationally published studies is not high (Pourhoseingholi et al., 2008; Dehkordi, Heydarnejad, & Fatehi, 2009; Safaee et al., 2009; Taleghani et al., 2009; Aghabarari et al., 2010). However, the number of longitudinal quantitative (Montazeri et al., 2008; Poorkiani et al., 2010; Bastani & Kiadaliri, 2011; Hatam et al., 2011) and qualitative (Harandi, 2010) studies in this area is scarce. The few studies that do exist indicate a decline in several dimensions of HRQoL. Interestingly, in parity with other studies not having a baseline before diagnosis, the study by Montazeri et al., (2008) with a baseline before diagnosis showed impairments in global QoL, pain, arm symptoms and body image even 18 months after treatment. In addition, most of the functional scales did not show improvement.

1.5   COPING WITH BREAST CANCER

The concept of ability to cope with illness (Fayers & Machine, 2007) and the context (Ashing-Giwa, 2004) can be important for how individuals rate their HRQoL. Women's perception of breast cancer experience might depend on how they cope with illness (O'Mahoney, 2001; Buik & Petrie, 2002; Kenne Sarenmalm et al., 2011).

Coping is the process of attempting to use one's thoughts and behaviors to manage the demands created by stressful events (Folkman, 2010). In this process a person seeks to manage, master, tolerate, reduce or minimize the demands of a stressful environment (Taylor & Stanton, 2007). Some coping resources (such as optimism, sense of mastery, self-esteem and social support) are suggested to aid this process (Taylor & Stanton 2007). A common theme in the coping process is related to the link of positive emotions to the individual's important values, beliefs and goals that comprise the individual's sense of meaning in life (Folkman, 1997). Coping, stressors and HRQoL outcomes probably covary, although how coping intervenes between stressors and HRQoL is not very clear (Yang, Brothers, & Anderson, 2008). However, coping may serve as a mediator in these relationships (Baron & Kenny, 1986).Testing the mediator effect of coping variables may contribute to the theoretical clarification of the role of coping (Yang, Brothers, & Anderson, 2008).

In the context of cancer, breast cancer is a significant stressor connected with experiences of different kinds of distress. Patients are thus often challenged to apply coping strategies to deal with this distress (Ben-Zur, Gilbar, & Lev, 2001; Wells 2008). Understanding how women with breast cancer cope with their diagnosis and different stages of illness is important for nurses in the recovery process (Wells, 2008). The results of two qualitative studies in Muslim women with breast cancer in Iran showed that spirituality and religious faith played a major role to adapt to the various problems associated with breast cancer (Taleghani, Yekta, & Nasrabadi, 2006, 2008). Hence, nurses need to recognize cultural differences in coping behaviors and provide culturally appropriate approaches to care (Emami, 2006). The findings of a literature review indicated that women with breast cancer are at risk of developing several psychological morbidities, including depression, anxiety, fatigue, negative thoughts, fear of dying, sense of aloneness, sexual and body image problems, as well as an overall decrease in HRQoL. Health care professionals should be aware of the different coping mechanisms that women use, such as positive cognitive restructuring, wishful thinking, emotional expression, disease acceptance, increased religious practice, family and social support and yoga and exercise. Integrating a coping ability in the care of women with breast cancer could constitute an important milestone in caring for patients with breast cancer (Al-Azri, Al-Awisi, & Al-Moundhri, 2009).

Hence, in order to have a holistic perspective in the measurement of HRQoL in patients with breast cancer, coping ability should be integrated and measured simultaneously. In this thesis, SOC, religious coping, and spiritual perspectives were selected to explore how women with breast cancer in Iran deal with their disease and find meaning in her life.

1.5.1   Sense of coherence (SOC)

According to Antonovsky coping ability and experience of health are connected to the individual's SOC and whether life stressors are experienced as comprehensible,

manageable and meaningful and whether the world is perceived as coherent (Antonovsky, 1987). Antonovsky (1987) hypothesized that SOC develops with increasing age and stabilizes by the end of young adulthood. SOC encompasses internal and external resources (generalize resistance resource, GRR). GRR refers to such thing as the characteristics of the person, the environment, social support, cultural stability and religion, all of which make available energy to cope with stressors. Antonovsky explained that an individual with a strong SOC has a greater coping capacity and more resources at hand to select adaptive and successful coping strategies (Antonovsky, 1987). He defines SOC as the extent of (a) structured and consistent beliefs regarding life (comprehensibility), (b) access to sufficient resources against stressful events (manageability), and c) belief and meaning to adjust to challenging situations (meaningfulness). In his view meaningfulness is a partly motivational construct that creates a sense "...that at least some of the problems and demands posed by life are worth investing energy in and commitment" (Antonovsky, 1987, p. 18).

Consideration to the concept of SOC in nursing has raised interest, not least in the area for caring of patients with cancer (Langius & Lind, 1995; Shapiro, 2001; Gibson & Parker, 2003; Ramfelt, Lutzen, & Nordström, 2005; Wettergren et al., 2004; Siglen et al., 2007; Bruscia et al., 2008; Sundberg et al., 2011) and specifically in women with breast cancer (Koinberg et al., 2006; Kenne Sarenmalm et al., 2011). A recent study showed that patients after the mastectomy with a higher SOC perceived themselves as having better functions (physical, emotional, cognitive and social) and less fatigue, less loss of appetite, fewer systematic side effects from treatment and breast symptoms, and fewer financial difficulties. Also, they reported less distress by body image and future perspective changes (Gerasimcik-Pulko et al., 2009).

In addition, studies within other populations show the same pattern regarding the role of SOC as a significant predictor of HRQoL: the stronger the SOC, the better the HRQoL (Eriksson & Lindström, 2007, Langius-Eklöf, Lidman, & Wredling, 2009). Furthermore, SOC has been shown to have a mediator (Wiesmann & Hannich, 2010; Braun-Lewensohn, Sagy, & Roth, 2011) or moderator (Richardson & Ratner, 2005) role, but the number of the studies in patients with cancer is small. The results of a study by Mullen, Smith, and Hill (1994) on cancer patients and spouses showed that higher SOC as a mediator contributed to more adaptive abilities and organized psychological stress.

Higher SOC with a stress buffering power may contribute to more adaptive abilities in specific situations (Antonovsky, 1987). SOC has been proposed to be a fairly stable dispositional characteristic of the personality (Antonovsky, 1987 page 186, 1993). Antonovsky also emphasized that SOC may point out minor changes in stressful situations, but fluctuations would be out of clinical relevance (Antonovsky, 1987).

1.5.2 Religious coping

Religion is another common and powerful way in which people cope with stressful situations (Burker et al., 2005). Religion and coping converge when individuals who have a religious orientation to life in general are faced with stressful life events (e.g., life-threatening illness) (Fox, 2002). Religious coping represents a key variable in research on health outcomes, not only because many individuals turn to their faith in times of illness, but also because studies have frequently found that religious coping might be associated with health outcomes (Cummings & Pargament, 2010). Pargament

(1997) suggested that an individual's general religious orientation increases his or her frequency in religious coping, which eventually leads to better face with stressful life events. When an individual confronts a stressful event, these general beliefs and practices interpret into specific forms of religious coping, and may mediate the outcomes of stressful life events. Religious coping strategies have also been divided into positive and negative subtypes (Pargament et al., 1998, 2000). Beyond providing a sense of global meaning in life, religious coping may help patients reframe their illness perception (Park, 2005).

Using religious coping strategies in the coping process during early stages of breast cancer appears to be common in the UK and health care professionals should be aware of more prevalent strategies (Thune-Boyle et al., 2011). The data from Muslim patients with breast cancer in Pakistan showed that religion and family support were two essential coping strategies (Banning et al., 2009; Ebadi et al., 2009). However, Zwingman et al., (2006) found that in a study on women with breast cancer in Germany positive religious coping could not predict demographic and cancer-related variables, however negative religious coping was correlated to age and living with a partner. Thus, negative religious coping was reported by older women and women without a partner. Further, a correlation between depression and religious coping was completely mediated by non-religious coping, indicating an indirect effect of both positive and negative religious coping on psychological adjustment of patients with breast cancer.

1.5.3 Spirituality

In the nursing literature, spirituality is defined as the essence or life principle of a person, i.e. as a scared journey, as the experience of the radical truth of things, or as a search for meaning and purpose in one's life (Cavendish et al., 2004). Reed (1986, 1987) explains it as spiritual perspective that is integral to, but not the same as, self-transcendence. The spiritual perspective includes the frequency, importance, and influence of spiritual discipline and a relationship to God or a higher power in daily living (Reed, 1992). Although the link between spirituality and health is not well understood, a higher spiritual perspective has been shown to have positive mental health benefits late in life (Reed, 1987, 1992). Living out in a spiritual perspective could be expressed in a person's life by engaging in private prayer or meditation, forgiving others, participating in corporate worship or seeking spiritual guidance in making decisions in everyday life (Cavendish et al., 2004).

Spirituality as a coping variable has been highly studied in recent and previous publications. The findings of a study on African-American survivors of breast cancer showed that symptom distress and spirituality were negatively and positively correlated respectively with HRQoL, indicating a major role of the nurses for assessing and providing culturally appropriate care to the patients. Furthermore, a study by Meraviglia (2006) supports the view that the aspects of spirituality, such as meaning in life and prayer lessen the impact of illness. These results corroborated the role of oncology nurses which is to provide holistic care and explore the aspects of spirituality in women diagnosed with breast cancer. Spirituality as a mediator variable has been previously studied with cancer patients (Nelson et al., 2009; Gall et al., 2009). Gall et al., (2009), for instance, found that spirituality (negative aspect) was a mediator of emotional distress of the patients with breast cancer through positive attitudes at two time points, the pre-diagnosis phase and 6 months after surgery.

1.6 RATIONALE

The foundation for this thesis is related to an interest to investigate HRQoL in women with breast cancer in Iran. Breast cancer in women in Iran like other middle-income countries occurs at least one decade younger than their counterparts in high-income countries. At the same time as advances in cancer care and treatment are ongoing, women diagnosed with breast cancer are confronted with a variety of distressing problems that may have an effect on physical, psychological, social, financial, and work-related life dimensions.

Discrepant results on HRQoL and its importance in women with breast cancer during treatment are found in the literature worldwide. In Iran there is no national mammography screening program for early detection of breast cancer. Thus, the possibility exists that women with breast cancer in Iran might have a more advanced disease than in Western countries.

In general, there is a lack of longitudinal studies having a baseline before the diagnosis of breast cancer which could serve as the basic reference value to interpret findings.

The strategies that women apply to cope with these challenges can be important in determining their HRQoL. Assessment of HRQoL over time together with coping abilities may contribute to new insights into how HRQoL of the women is influenced by their breast cancer and identify important needs of the women that can be prevented during the cancer trajectory.

2 AIMS

The overall aim of the thesis was to investigate HRQoL and its determinants in women with breast cancer before final diagnosis and 6 months later in order to increase our knowledge about the planning of supportive care and nursing interventions in Iran. The specific aims of the thesis were:

- To translate the HI, SOC scale, Brief RCOPE scale and SPS into the Persian language and to test their validity and reliability within the Iranian culture (Study I).

- To investigate the factorial structure, convergent validity and reliability (in the form of internal consistency, stability and robustness) of the SF-12v2 in a healthy Iranian sample, following translation and establishment of content and face validity (Study II).

- To investigate the pattern of changes in HRQoL dimensions (functional and symptom scales of HRQoL and well-being) and coping abilities (the SOC, spirituality and positive and negative RCOPE) in a group of suspect women for breast cancer at pre-diagnosis and 6 months later in comparison with a control group and to explore predictors of HRQoL dimensions in the breast cancer patients at the 6-month follow-up (Study III).

- To examine the mediating effect of SOC (6 months after the pre-diagnosis of breast cancer) on correlation between baseline HRQoL dimensions and the same dimensions at the 6-month follow-up in a sample of women with breast cancer in Iran (Study IV).

3 METHODS

3.1 DESIGN

The design of this thesis was conducted using a quantitative approach. The first two studies (Study I and Study II) are cross-sectional and methodological. In these studies translation of five self-rated instruments into the Persian language and psychometric analyses were performed. Study III and IV are longitudinal studies with a clinical perspective. Study III used a prospective and comparative design. In this third study HRQoL dimensions and coping abilities were measured in a sample of women with breast cancer and then compared with a control group of women seeking mammography screening and later not diagnosed with breast cancer at two time points: baseline before final diagnosis of breast cancer (T1) and 6 months later (T2). Study IV used a prospective design to assess the role of SOC as a mediator of HRQoL at T2. Data for this study were obtained from the sample of women with breast cancer in Study III. The four studies included in this thesis are presented in Table 1.

Table 1. Summary of design, samples, instruments and data analyses in the thesis

Study	Design	Samples	Instruments	Data analysis
I	Descriptive and cross-sectional	Healthy people (T1) n=333 and (T2) n=298 Healthy participants and women with breast cancer for face validity (n=20)	HI, SOC, SPS and Brief RCOPE	Descriptive statistics, Pearson correlation coefficient, intra-class correlation coefficient, Cronbach's alpha coefficient, item-total analysis, hierarchical multiple regression analysis
II	Descriptive and cross-sectional	Healthy people (T1) n=252 and (T2) n=203 Healthy participants and women with breast cancer for face validity (n=20)	SF-12v2, SOC, and HI	Descriptive statistics, Student's paired t-test, intra-class correlation coefficient, Cronbach's alpha coefficient, EFA, SEM using Lisrel 8.80
III	Longitudinal and comparative	Women with breast cancer (n=162) Control women (n=639)	EORTC QLQ-C30, QLQ-BR23, HI, SOC, SPS and Brief RCOPE	Descriptive statistics, Chi-square, Student's paired t-test, independent Student's t- test, effect size, mixed ANOVA, hierarchical multiple regression analysis
IV	Longitudinal and prospective	Women with breast cancer (n=162)	EORTC QLQ-C30, SF-12v2, HI, and SOC	Descriptive statistics, Pearson correlation coefficient, mediational analysis (three hierarchical multiple regression analysis, Sobel test, and Bootstrap)

3.2 PARTICIPANTS

3.2.1 Healthy sample (Study I)

A convenience sample of healthy women and men (n = 375) employees working in nine urban health centers (n = 210), two universities (n = 136) and one private company (n = 29) in Tehran participated in Study I. All participants had to meet the following inclusion criteria: aged 18 years or older, free from chronic disease, literate in the Persian language and of Iranian nationality. At the health centers, health care providers, clerical personnel and trained community health volunteers were approached. Teachers from the universities and clerical personnel from a private company were recruited. The healthy sample participated at baseline and one month later in this study. Dropout rates ranged from 42 (11.2% participants who did not complete or return the package of the instruments at T1) to 35 (9.3% participants who declined further participation at T2).

3.2.2 Healthy sample (Study II)

A convenience sample of 289 healthy respondents from Study I was recruited. The participants in Study I belonging to the universities not situated in the area of residence of the author were excluded (n=106). Subsequently in Study II the participants came from nine urban health centers (n = 210), one university (n = 30) and a private company (n = 49) in Tehran. They participated at two time points (baseline and one month later). Dropout rates ranged from 37 (12.8%) participants who did not complete or return the instrument at T1 to 49 (16.9%) participants who declined further participation at T2.

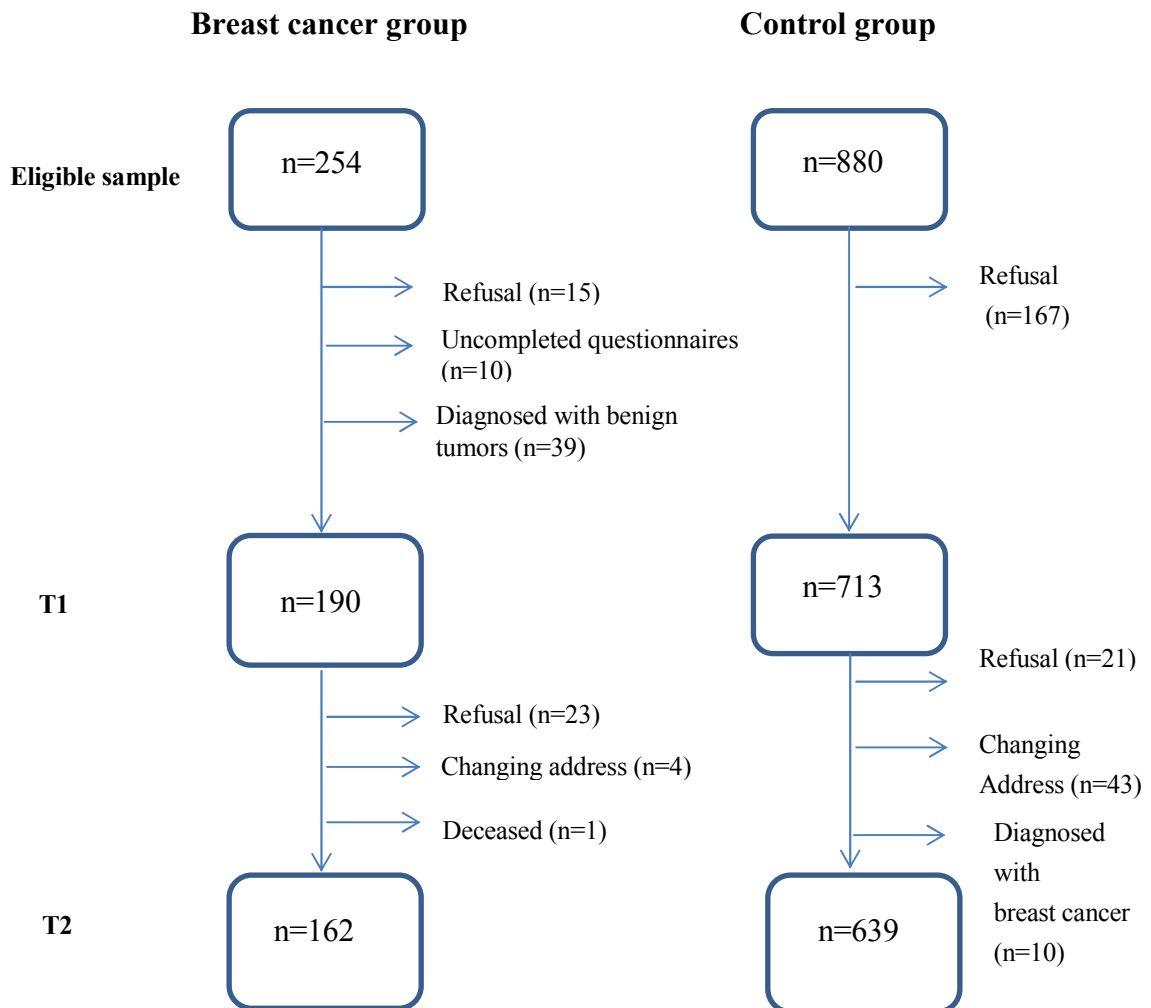### 3.2.3 Sample for face validity (Study I & II)

Twenty volunteer participants were selected to assess the face validity of the instruments: 5 healthy persons from one of the urban health centers, 5 healthy persons from one of the universities and 10 women with breast cancer from one educational hospital.

3.2.4 Breast cancer group (Study III & IV)

A prospective sample of 254 women with a suspect lump in the breast or other symptoms was approached before final diagnosis at the surgical wards of two hospitals belonging to Tehran University of Medical Sciences. Of the 254 eligible women who met the inclusion criteria (to have sufficient knowledge of the Persian language to answer the questionnaires, and having no previous cancer history), 92 (36.2%) dropped out by to the end of the 6-month follow-up (T2). Fifteen (6%) women refused to participate, 10 (4%) did not complete all the questionnaires and 39 (15%) were diagnosed with benign tumors after surgery. Hence, the final sample at baseline (pre-diagnosis, T1) consisted of 190 (75%) women with breast cancer. At T2, 23 women (9%) declined further participation, 4 (2%) had a change of address and 1 (0.4%) had deceased. Thus, the final sample at T2 consisted of 162 (64%) women with breast cancer (Figure 1). The participants were from all parts of Iran.

3.2.5 Control group (Study III)

Totally, 880 women with sufficient knowledge of the Persian language to answer the questionnaires and no previous cancer history were randomly selected (certain days per week) from the mammography wards of the same two hospitals as a control group before undergoing mammography/sonography. These women came to the mammography wards by referral from a physician based on their own initiative or a physician. Of these 880 eligible women, 167 (19%) women did not return the package of instruments, leaving 713 (81%) at T1. At T2, 21 (2%) women declined further participation, 43 (5%) had an unknown address and 10 (1%) were diagnosed with breast cancer. Therefore, the final sample was made up of 639 (73%) women (Figure1).

Breast cancer group　　　　**Control group**

Eligible sample

n=254　　　　　　n=880

Refusal (n=15)

Refusal
(n=167)

Uncompleted questionnaires
(n=10)

Diagnosed with benign
tumors (n=39)

T1　　n=190　　　　　n=713

Refusal (n=21)

Refusal (n=23)

Changing
Address (n=43)

Changing address (n=4)

Deceased (n=1)

Diagnosed
with
breast cancer
(n=10)

T2　　n=162　　　　　n=639

Figure 1. Sampling for the women with breast cancer (Study III & IV) and control group (Study III).

3.3 INSTRUMENTS

In this thesis several self-rated international well-known instruments were used to measure HRQoL dimensions and coping abilities. The EORTC QLQ-C30 and QLQ-BR23 were already translated and tested in the Persian language (Montazeri et al., 1999, 2000), but the others were not available in Persian. They were therefore translated into the Persian language and thereafter psychometrically investigated.

3.3.1 The EORTC QLQ-C30 and BR23 (Study III & IV)

HRQoL was measured using the validated Persian versions of two worldwide questionnaires: the EORTC QLQ-C30 (version 3) (Montazeri et al., 1999) and the EORTC QLQ-BR23 (Montazeri et al., 2000). The EORTC QLQ-C30 with 30 items is a core cancer-specific questionnaire that consists of a global health status/QoL scale, five functional scales (physical functioning, PF, role functioning, RF, emotional functioning, EF, cognitive functioning, CF and social functioning, SF), three symptom scales (fatigue, FA, pain, PA and nausea/vomiting, NV) and six single items (appetite loss, AP, insomnia, SL, dyspnea, DY, constipation, CO, diarrhoea, DI and financial difficulties, FI). The EORTC-QLQ-BR23 is a disease-specific module for breast cancer with 23 items. It includes two functional scales (body image, BI, and sexual functioning, SEF), three symptom scales (breast symptoms, BS, arm symptoms, AS and systemic side effects, ST) and individual items (sexual enjoyment, SEE, hair loss, HL and future perspective, FU). Both the EORTC QLQ-C30 and EORTC QLQ-BR23 are rated on a four-point scale from 1 to 4, except for global health status/QoL in the EORTC QLQ-C30, where a seven-point scale is applied. All of the scales and single-item measures are converted to scores from 0 to 100. A high score on the global health status/QoL and functional scales indicates high HRQoL and functioning. A high score for symptom scales or single items represents a high level of symptoms. The validity and reliability of these questionnaires have been studied extensively and supported in various countries (Aaronson et al., 1993; Montazeri et al., 1999, 2000).

3.3.2 The Short Form 12-ITEM Health Survey Version 2 (Study II & IV)

The SF-12v2 is a short form (SF), multi-purpose and generic measurement of health status which applies a Likert-Scale format (Ware et al., 2002). Psychometric properties of the SF-12v2 have been determined in previous studies (Ware et al., 2002; Lee, Browell, & Jones, 2008; Cheak-Zamora, Wyrwich, & McBride, 2009). The SF-12v2 consists of a 12-item subset of the SF-36 version 2 (SF-36v2) classified into eight dimensions: bodily pain (BP), general health (GH), vitality (VT) and social functioning (SF) with one item each. In addition, physical functioning (PF), mental health (MH), role physical (RP) and role emotional (RE) dimensions are indicated with two items each (Ware et al., 2002). According to a theoretical test of the original model, the PF, RP, BP and GH scales render a physical component summary (PCS) measure while, the MH, RE, VT and SF scales yield a mental component summary (MCS) measure (Ware et al., 1996). In this thesis a standard 4-week recall period version was used. Scores of PCS and MCS measures are estimated by using the 12 items through scoring algorithms with weighted item response. Summary measures are standardized to produce a mean of 50 with a standard deviation of 10 for the United States (US) population (norm-based scoring). The eight scales of the SF-12v2 are calculated using the transformed scores (range: 0-100), where the higher the score, the better the perceived health (Ware et al., 1996, 2002). By applying the US standard scores, results

can simply be compared from various countries and settings. Further, comparisons within one country can be conducted by parallel analyses or country-specific scoring. A License agreement for using the SF-12v2 was acquired from QualityMetric Incorporated (# 2576 May 2006; #36170 June 2008).

3.3.3 The Health Index (Study I, II, III & IV)

The HI has been developed in Sweden (Nordström, Nyman, & Theorell, 1992; Forsberg & Björvell, 1993) and comprises nine items (energy, mood, fatigue, loneliness, sleep, dizziness, bowel function, pain and mobility). Each item is rated on a four-point verbal category scale and items are added to obtain a total score in an index with a range from 9 to 36. The higher the score, the better the perceived general health and well-being. The psychometric properties of the HI have proved to be satisfactory (Nordström et al., 1992; Forsberg & Björvell, 1993; Sjöström, Langius-Eklöf, & Hjertberg, 2004).

3.3.4 The Sense of Coherence Scale (Study I, II, III & IV)

Antonovsky (1987) developed the SOC scale to assess the concept of SOC. The short form of the SOC scale consists of 13 items. The respondents indicate agreement or disagreement on a seven-point semantic differential scale with two anchoring responses. The total score can range from 13 to 91, where higher scores indicate higher SOC (Antonovsky, 1987). The SOC scale has been used in at least 33 languages and found to have satisfactory results concerning validity and reliability as well as cross-cultural applicability (Eriksson & Lindström, 2005).

3.3.5 The Spiritual Perspective Scale (Study I & III)

The SPS was developed by Reed (1986, 1987) to measure the participants' views of spiritual values and engagement in spirituality interactions. It has 10 items organized on a verbal scale ranging from 1 to 6, where a higher score represents a greater spiritual perspective. The scores of the 10 items are added to give a total score ranging from 10 to 60. The SPS has been tested for psychometric properties within different samples (Reed, 1986, 1987; Jesse & Reed, 2004; Dailey & Stewart, 2007).

3.3.6 The Brief Religious Coping Scale (Study I & III)

The Brief RCOPE, which was developed by Pargament et al., (1998), comprises 14 items rated on a four-point scale that discriminate between positive and negative RCOPE: 7 items represents the positive RCOPE scale and 7 items the negative RCOPE scale (Pargament et al., 1998). Positive RCOPE represents a secure relationship with God, whereas negative RCOPE indicates a religious struggle that develops out of a weaker relationship with God (Pargament et al., 2004). The scoring range for each scale is from 7 to 28, with higher scores indicating stronger positive/negative RCOPE. The validity and reliability of the Brief RCOPE are supported in several studies (Pargament et al., 1998, 2000).

3.3.7 Demographic and clinical data

Demographic data (sex, age, marital status, working status and educational level) were collected using a short interview by a questionnaire sheet at the first visit in all studies. Clinical data for the breast cancer group were acquired from medical records (menopause, comorbidity, cancerous body side, biopsy before surgery, surgery type, cancer stage and treatment type) (Study III & IV) and for the control group by a self-report questionnaire (menopause and comorbidity) (Study III).

3.4 DATA COLLECTION PROCEDURES

3.4.1 Study I and II

An invitation letter, together with the inclusion criteria, was posted on the walls at the two universities, nine health centers and the private company during three working days. This announcement was directed to the recruitment of healthy participants at each place, where the aim of the study, voluntariness and confidentiality were emphasized. When participants stated their interest and agreement to participate, detailed written information was given to the participants and written informed consent was subsequently obtained. The participants received the package of instruments (HI, SOC, SPS, Brief RCOPE and SF-12v2) at an appointed place. They were requested to respond to the questionnaires within 3 days, and thereafter leave the package of the instruments to the same place or to the researcher. The same procedure was followed 1 month later.
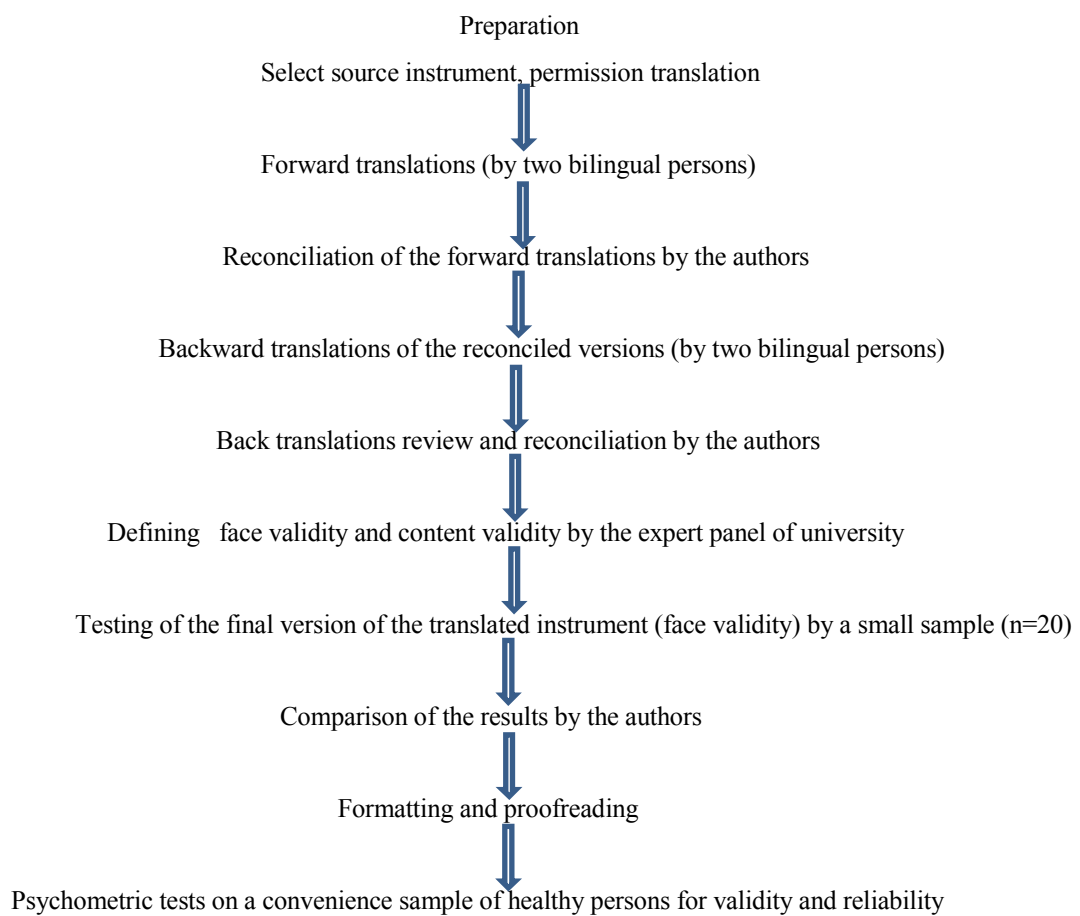
3.4.2 Study III and IV

At the surgical wards, baseline data (T1) for the breast cancer group (Study III and IV) were collected using the EORTC QLQ-C30, SOC, HI, SPS, Brief RCOPE and SF-12v2. This was done before final diagnosis of breast cancer (this phase includes 1-14 days before surgery). The breast cancer diagnosis was confirmed based on the pathology report during surgery and followed by a final report 2 or 3 weeks later. Six months later (T2), the same questionnaires, in addition to the EORTC QLQ-BR23, were mailed to the participants. A letter of explanation and a pre-stamped envelope accompanied the questionnaires. In the control group (Study III) baseline data (T1) were collected at the mammography wards before the mammography/sonography examination using the EORTC QLQ-C30, SOC, HI, SPS, Brief RCOPE and SF-12v2. Six months later (T2), the same questionnaires together with a letter and a pre-addressed and stamped return envelope were mailed to the participants.

At baseline, the instruments were distributed among the participants in the surgical and mammography wards and were collected 2-3 days later. To increase the response rate and minimize the risk of attrition, a reminder (via telephone) was issued for those participants who did not return the package after 10 days.

3.5 TRANSLATION PROCEDURE (STUDY I & II)

A standard guideline was used for translation and cultural adaptation (Brislin, 1970; Jones, et al., 2001; Maneesriwongul & Dixon, 2004) of the English versions of the SOC, Brief RCOPE, SPS and SF-12v2, as well as the Swedish version of the HI into the Persian language. This process included simultaneous translations and blind back-

translations, followed by expert panel evaluation and pilot testing (Brislin, 1970; Jones et al., 2001; Maneesriwongul & Dixon, 2004). For cultural adaptation, face and content validity of the translated instruments were assessed by the expert panel of university of medical sciences in Iran. After that all versions of the translated instruments were reconciled by the authors and a symmetrical translation via loyalty to the meaning of the HI, SOC, Brief RCOPE, SPS and SF-12v2 was produced. Further face validity of the instruments was estimated by 20 volunteers of healthy participants and women with breast cancer. The process of translation and cultural adaptation of the instruments in this thesis (Study I & II) is depicted in Figure 2.

Preparation

Select source instrument, permission translation

Forward translations (by two bilingual persons)

Reconciliation of the forward translations by the authors

Backward translations of the reconciled versions (by two bilingual persons)

Back translations review and reconciliation by the authors

Defining   face validity and content validity by the expert panel of university

Testing of the final version of the translated instrument (face validity) by a small sample (n=20)

Comparison of the results by the authors

Formatting and proofreading

Psychometric tests on a convenience sample of healthy persons for validity and reliability

Figure 2. Translation procedure and cultural adaptation of the instruments in Study I and II.

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3.6   DATA ANALYSES

All statistical analyses were conducted using the Statistical Package for Social Science (SPSS) versions 13-20. For analysis of some parts of the data in Study II, Lisrel 8.80 was used.

3.6.1   Validation of the instruments (Study I & II)

Different types of validity were estimated in this thesis, including face, content, criterion-related, convergent and construct validity. An expert panel of university teachers assessed the face and content validity of the HI, SOC, SPS, RCOPE and SF-12v2. Moreover, 20 healthy and diseased volunteer were engaged to test the face validity of the instruments. Content validity index for scale (S-CVI) was estimated for the SF-12v2. The relevance, clarity and simplicity of the individual items of the SF-12v2 were evaluated by CVI assessment on a four-point scale. A value of ≥ 0.80 constitutes a good content validity (Polit & Beck, 2008).

For testing the criterion-related validity of the instruments (Study I) 10 hypotheses were proposed based on the strength of reliable evidence concerning the association among the SOC scale, the HI, the SPS and the Brief RCOPE: main hypotheses (when two instruments had earlier been used together) and exploratory hypotheses (when similar concepts are measured in relation to each other). The Pearson correlation coefficient was used and a correlation below 0.20 was considered low, between 0.20-0.35 slight, 0.36-0.65 moderate, 0.66-0.85 high and ≥ 0.86 very high (Cohen, Morison, & Manion, 2000). Moreover, the criterion-related validity of the instruments was estimated by applying hierarchical multiple regression analyses at T1 and T2. The HI scores were treated as a dependent variable. The SOC, SPS, positive and negative RCOPE scores were included in the hierarchical multiple regression models as independent variables because they are viewed as more robust measures (trait). Independent variables were classified into the five categories: significant demographic variables (age, sex, education, marital status and job status), SOC, positive RCOPE, negative RCOPE and SPS scores. The demographic variables were controlled and entrance of the remaining independent variables into the regression models was ordered according to a higher correlation coefficient with HI scores.

Construct validity of the SF-12v2 (Study II) was estimated by factorial and convergent validity. Factorial validity of the SF-12v2 was measured by both exploratory factor analysis (EFA) and structural equation modeling (SEM) at T1. Hence, EFA and SEM were carried out on the 12 items and eight scales of the SF-12v2 to test each factor structure, respectively. According to the original SF-12 conceptual model (Ware et al. 1996) and studies on items/scales cross-loadings (Ware, 2002), it was hypothesized that a model with the following features would fit with the SF-12v2 data: (1) the model would contain a two-factor structure, comprising the PCS and MCS measures (2) loadings of the items and scales on the factors would be uniform with the original version (PCS: GH, PF, RP, BP and MCS: RE, MH, VT, SF) and (3) cross-loadings of the GH, VT and SF items and scales might be found. Cross-loadings were regarded as substantial if they were greater than 0.40 (Ware, 2002). EFA was conducted using principal component analysis (PCA) with varimax and oblique rotations. For more specific testing of the confirmation of the factor structure, a confirmatory factor analysis (CFA) was run by SEM with four models. In line with the theoretical model of the SF-12 (Ware et al., 1996), model 1 contained two latent inter-correlated factors (PCS and MCS), in which each factor correlated to the six specific items. Model 2

included two latent inter-correlated factors, in which each factor correlated with the four specific scales (PCS: GH, PF, RP, BP and MCS: RE, MH, VT, SF). Cross-loading between the items and scales of the SF-12v2 was assessed by models 3 and 4, which were created in the same way as models 1 and 2, but with cross-loadings. Occasionally, models created using CFA make it so that some items/scales have a loading of zero on the opposite component, which inhibits inconsistency (Fleishman, 2010). By using the Lisrel programme and fixing the models with corresponding factor loadings, two paths were omitted in models 3 and 4 (in model 3 two paths from the PCS measure to the MH1 scale and from the MCS measure to the PF1 scale; and in model 4 two paths from the PCS measure to the MH scale and from the MCS measure to the PF scale). Specific indices and cutoff points were considered for the results of the CFA by SEM analyses: Chi-square to the degrees of freedom ratio (criteria: ratio < 6), comparative fit index (CFI) (criteria: > 0.90), standardized root mean square residual (SRMR) (criteria: < 0.08), non-informed fit index (NNFI) or Tucker-Lewis index (criteria: > 0.90) and incremental fit index (IFI) or BL89 (criteria: > 0.90). Further, improvements in the models fit were evaluated by a decrease in the Akaike information criterion (AIC) and the expected cross-validation index (ECVI) (Hurley et al., 1997; Hu & Bentler, 1998; Chen, 2007).

In support of convergent validity, associations between the scores of the PCS and MCS measures with the SOC and HI scores were evaluated by the Pearson correlation coefficient. Based on previous results (Söderman et al., 2002; Wettergren et al., 2004; Von Lengerke, Janssen, & John, 2007), slight to moderate positive associations between the concepts of SOC and HI scores with the PCS and MCS measures were hypothesized.

3.6.2 Reliability of the instruments (Study I & II)

Three approaches were used to measure the reliability of the instruments: (1) internal consistency (Study I and II), (2) item-total analysis (Study I), and (3) test re-test (Study I and II).

Internal consistency was estimated using Cronbach's alpha coefficient. A Cronbach's alpha coefficient ≥ 0.70 was considered acceptable (Nunnally & Bernstein, 1994). The inter-item correlation analysis was carried out by computing the corrected item-total correlation for the items (Furr & Bacharach, 2008) where a value of ≥ 0.30 was considered reasonable (Ferketich, 1991).

The intra-class correlation coefficient (ICC) was applied for the test re-test reliability, with values > 0.80 regarded as excellent reliability (Nunnally & Bernstein, 1994). However, most QoL questionnaires fail to attain a demanding level for ICC and therefore some authors recommend that values ≥ 0.60 are reasonable (Fayers & Machine, 2007). In addition, statistical changes in the means of two summary scores and eight scales of the SF-12v2 were evaluated by paired t-test between T1 and T2 (Study II).

3.6.3 Study III

Study outcomes (HRQoL dimensions, HI, SOC, SPS and positive and negative RCOPE) were evaluated by P-P plots (the normality assumptions of most variables were not violated). Mean differences within and between groups were assessed by

dependent and independent Student's t tests, respectively. The differences within each group were estimated by effect size and interpreted by Cohen's criteria: none < 0.20, small 0.20-0.49, moderate 0.50-0.79 and large $\geq$ 0.80 (Fayers & Machine, 2007). A correlation matrix was computed to estimate which variables to include in multiple analyses and comorbidity fell out most frequently as the strongest variable. Mixed analyses of variance (ANOVAs) with comorbidity as a covariate were calculated to determine the interaction effect between time and group on the outcome variables. The scores were converted into 0-100 scales and then differences in changes of the estimated mean scores were calculated over time and used as criteria for impairment or improvement. Clinical significance changes in self-reported instruments are interpreted in terms of small (5-10), moderate (11-19) or large changes ($\geq$ 20) (Osoba et al., 1998). The hierarchical multiple linear regression analyses were run to estimate the predictors of the EORTC QLQ-C30 and HI scores in the breast cancer group at the 6-month follow-up. Independent variables were grouped into four blocks: (1) demographic variables (age, marital status, education and working status), (2) clinical variables (menopause, comorbidities, biopsy before surgery, surgery type, stage of cancer and treatment types), (3) coping variables (SOC, SPS and positive and negative RCOPE) and (4) baseline scores for each dependent variable (EORTC QLQ-C30 dimensions, in addition to HI).

3.6.4 Study IV

First, calculations of the Pearson product moment correlation coefficients to test bivariate relationships of the mediator (SOC-T2), dependent variables (HRQoL-T2 dimensions), and independent variables (HRQoL-T1 dimensions) were performed. A general mediational model was then designed to test the study hypothesis. Based on Baron and Kenny's (1986) rules, a series of hierarchical multiple regression analyses was conducted on 13 statistical mediational models. Age as a continuous variable and educational level and cancer stage as dichotomous variables were controlled for in all analyses. A mediation potential effect of SOC was tested by three equations in regression tests. In the first equation it was examined whether (1) the independent variable (HRQoL dimensions at T1) was significantly correlated with the mediator (the degree of SOC at T2); in the second equation (2) it was determined whether the independent variable (HRQoL dimensions at T1) was significantly correlated with the dependent variable (HRQoL dimensions at T2); and, in the third equation (3) it was studied whether the mediator (the degree of SOC at T2) significantly correlated with the dependent variable (HRQoL dimensions at T2) when controlling for the independent variable (HRQoL dimensions at T1). If significant results ($p < 0.05$) were found for all three regression tests in a model, the Sobel test was then estimated to evaluate the significant meditational or indirect effect. A value of more than 1.96 (p <0.05) indicates support for mediation (Preacher & Hayes, 2008). For further verification of the mediational effect, the bootstrap method was used to test equation three of the regression analysis (Austin, 2008). Thus, final decision was established based on the results of the bootstrap. In this study, the bootstrap was estimated by 1000 bootstrap samples and with bias-corrected accelerated method to estimate the 95% confidence interval (CI). If this estimation does not include zero, it suggests the significant mediation effect at the 0.05 level (Firtz & Mackinnon, 2007; Rucker et al., 2011). The degree of SOC is a total mediator if the correlation between the independent (HRQoL dimensions at T1) and dependent variable (HRQoL dimensions at T2) is non-significant. However, the degree of SOC is a partial mediator if there is a reduction in

the correlation. According to Cohen & Cohen (1988) R^2 as small as 0.10 (effect size = 0.11) in a multiple regression analysis with five independent variables is optimal and meets the power of 0.90 for a sample size of 154 breast cancer patients. Therefore, our sample size (n = 162) seems sufficient for testing the hypothesis.

4 ETHICAL CONSIDERATIONS

The thesis, including the four empirical studies (I-IV), was approved by the National Ethical Board of Research at the Ministry of Health and Medical Education in Tehran, Iran. The project followed the Helsinki Convention. All participants were given verbal and written information about the study, including the aims, methods and procedures of the studies. In addition, the participants were told that participation is voluntary and that they could withdraw at any time without consequences. The participants were also given the name and phone number of the researcher. Each participant received a code number that was entered into the data files. The code list was locked in a room not linked to the computer with the files. The researcher only knew the code list. During analysis and reporting of the results, confidentiality and precision of the reported information were considered carefully.

Some ethical dilemmas should be mentioned. Initially, when the researcher approached the prospective sample of 254 women with a suspect lump or other symptoms in the breast, it was a vulnerable period in their life. Thus, the researcher attempted to be sensitive to the subtle psychological consequences of participating in this study and protect the participants from psychological harm (e.g., stress, fear and anxiety) by initiating communication in a careful and thoughtful manner and by presenting a clear description regarding the nature of the study and the participant`s right to withdraw from further participation at any stage. All participants (women with breast cancer, control women and healthy samples) had access to the researcher throughout of the study.

Furthermore, some women might perceive some questions as encroaching on their integrity, but the researcher's experience was that most of the participants, especially those who are threatened with a cancer diagnosis, preferred to have knowledge of their situation.

5 RESULTS

5.1 CHARACTERISTICS OF THE SAMPLES

5.1.1 Healthy sample (Study I)

The mean age of the participants was 38.2 years (SD = 10.8 years). The majority of the participants were female (78%). More than 70% of the participants were married and nearly 63% were employed (Table 2).

5.1.2 Healthy sample (Study II)

Socio-demographic characteristics of the 203 healthy Iranian participants who participated at baseline (T1) and 1 month later (T2) are listed in Table 2.

Table 2. Demographic characteristics of the healthy participants in study I (n= 298) & II (n=203).

Variables	study I n (%)	study II n (%)
Sex		
Female	233 (78)	156 (77)
Male	65 (22)	47 (23)
Marital status		
Single	75 (25)	40 (20)
Married	210 (71)	153 (75)
Divorced/widowed	13 (4)	10 (5)
Job status		
Housewife	84 (28)	78 (38)
employed	188 (63)	111 (55)
Student	23 (8)	11 (5)
Retired	3 (1)	3 (2)
Educational level		
Primary school	15 (5)	16 (8)
Secondary school	23 (8)	21 (10)
High school	18 (6)	19 (9)
College/university	142 (81)	148 (73)

5.1.3 Women with breast cancer and control group (Study III & IV)

The mean age of the women with breast cancer (M = 46.1 years, SD = 10.2 years, range 23-71 years, n = 190) and the mean age of the women in the control group (M = 47.4 years, SD = 8.6, range 21-80 years, n = 713) did not differ significantly at baseline. Personal characteristics of these samples are presented in Table 3, respectively.

Table 3. Personal characteristics of the sample of women with breast cancer (n=190) and control group (n = 713) at baseline (study III).

Demographic & clinical variables	Breast cancer group n (%)	Control group n (%)	df	p [a]
Marital status			2	0.391
Single	14 (4.7)	46 (6.5)		
Married	151 (79.5)	586 (82.2)		
Divorced	9 (4.7)	33 (4.6)		
Widowed	16 (8.4)	48(6.7)		
Education			1	0.091
Primary school	31 (16.3)	139 (19.5)		
Secondary school	28 (14.7)	102 (14.3)		
High school	6 (3.2)	51 (7.2)		
Diploma	66 (34.7)	248 (34.8)		
University	59 (31.1)	173 (24.3)		
Working status			2	0.001
Housewife	115 (60.5)	501 (70.3)		
Employed	60 (31.6)	143 (20.1)		
Retired	15 (7.9)	69 (9.7)		
Menopause			1	0.397
Yes	69 (36.3)	283 (39.7)		
No	121 (63.7)	430 (60.3)		
Comorbidities [b]			1	0.000
Yes	84 (44.2)	575 (80.6)		
No	106 (55.8)	138 (19.4)		

[a] Differences between groups' proportions were tested by chi-square statistics.
[b] Comorbidities: chronic diseases such as diabetes, hypertension and musculoskeletal problems.

5.1.4 Clinical characteristics of women with breast cancer

During the baseline stage, the women had not been informed about their final diagnosis. All women with breast cancer had surgery that was followed by one, two or three adjuvant treatments: 148 (78%) chemotherapy, 142 (75%) radiotherapy and 115 (60%) hormonal therapy. Adjuvant breast cancer treatment-Herceptin as part of the treatment course of chemotherapy was used in nine (7%) women with breast cancer. The majority of women with breast cancer (76%) received $\geq$ 6 chemotherapy courses. Duration of chemotherapy in the present study was 3 months or longer, which was started between 20 to 30 days after surgery with 3-week intervals between treatments. Further, external radiotherapy was conducted with 50 Gy in 25 fractions (10 Gy as boost dose). Tomoxifen was used as the most common hormonal medicine (87%) for oestrogen receptor positive breast cancer (ER+) in pre- and post-menopausal women; the remaining ER+ women (n = 14, 12.6%) were prescribed other types of hormonal medicine (Table 4).

Table 4. Medical characteristics of the sample of women with breast cancer in study III (n = 190).

Variable	n	Percent (%)
Breast cancer		
One side	185	97.4
Two sides	5	2.6
Biopsy before surgery		
Yes	108	56.8
No	82	43.2
Type of surgery		
Breast conservation	86	45.3
Mastectomy	102	53.7
Missing	2	1.1
Stage at diagnosis		
0	5	2.6
I	39	20.5
II	87	45.9
III	47	24.7
IV	4	2.1
Undefined	4	2.1
Missing	4	2.1
Chemotherapy		
Yes	148	77.9
No	40	21.1
Missing	2	1.1
Radiotherapy		
Yes	142	74.7
No	42	22.1
Missing	6	3.2
Hormonal therapy		
Yes	115	60.5
No	57	30.0
Missing	18	9.5

5.2   PSYCHOMETRICS OF THE SCALES IN STUDY I

5.2.1 Validity

The results of the criterion-related validity assessment demonstrated that from the 10 formulated hypotheses, three main hypotheses were confirmed: hypothesis 1 (moderate positive correlation between the SOC scale and the HI) and hypothesis 2 (slight positive correlation between the SOC scale and the SPS). Whereas hypothesis 3 (low positive correlation between the positive and negative RCOPE scales) was rejected but the correlation was very close to the criteria. Further, three exploratory hypotheses were accepted: hypothesis 2 (moderate inverse correlation between the SOC scale and the negative RCOPE scale), hypothesis 4 (slight negative correlation between the HI and the negative RCOPE scale) and hypothesis 5 (moderate positive correlation between the SPS and positive RCOPE scale). Thus, evidence was found for the criterion-related validity of these instruments. Clarification of the results of the criterion-related validity was performed by hierarchical multiple regression analyses. The results of the regression analyses showed that the scores of the SOC scale both at T1 ($\hat{\beta} = 0.52$, p<0.001) and T2 ($\hat{\beta} = 0.58$, p < 0.001) were a stronger predictor of HI scores than the SPS and RCOPE scales. Together, age, gender, SOC, negative and positive RCOPE and SPS accounted for 37% of the explained variance in the HI scores at T1. Age, SOC and negative RCOPE explained 41% of the variance in the HI scores at T2.

5.2.2 Reliability

The reliability results revealed that the test-retest (≥ 0.80) and Cronbach's alpha coefficients (> 0.70) of the HI, SOC scale, SPS and Brief RCOPE scale were acceptable. The item analysis indicated that the items of the instruments could distinguish individuals with a high score from those with a low score on the total test scores (≥ 0.30), except for item 1 of the SOC scale (Do you have the feeling that you don't really care about what goes on around you?) and item 7 of the negative RCOPE scale (Questioned the power of God). Regarding the type of responses to items 1 and 7, 73.3% and 79% of the respondents at T1 and T2, respectively, reported that they did not care about what went on around them (SOC item 1, response alternatives 5, 6 and 7). Furthermore, 92.9% of the respondents at T1 and 93.9% at T2 mentioned that they never questioned the power of God (RCOPE negative scale item 7, response alternative 1). After deleting item 1 of the SOC scale and item 7 of the negative RCOPE scale, Cronbach's alpha remained within the criteria of > 0.70.

5.3 PSYCHOMETRIC PROPERTIES OF THE SF-12V2 (STUDY II)

5.3.1 Validity

S-CVI (85.6%) and face validity of the instrument were acceptable. The EFA results with PCA by varimax and oblique rotations that included 12 items and 8 scales explained a two-factor conceptual structure (the PCS and MCS measures). The PCS and MCS measures together with the 12 items and 8 scales explained 59.3% and 64.0% of the total variance, respectively. The results of the EFA with oblique rotation showed similarity to the varimax rotation, the GH loaded more on the mental component than on the physical component but no cross-loading was observed. Further exploration using SEM analyses with four models was performed. The SEM results showed that all models exceeded the sensitivity criteria regarding goodness of fit (X^2/df, CFI, SRMR, NNFI, IFI).The factor loadings in these models indicated that all variables were more highly loaded on the respective components (mental and physical), excluding model 3 (two-factor solution with 12 items and cross-loading between them) and model 4 (two-factor solution with eight scales and cross-loading between them), which demonstrated that the GH was loaded more on the mental component. The variance explained by the four models of the Iranian version of the SF-12v2 was 0.85 (model 1), 0.94 (model 2), 0.87 (model 3) and 0.98 (model 4). Models 2 and 4 demonstrated the best fit according to the AIC and ECVI results. The scores of the PCS and MCS measures were significantly ($p < 0.001$) correlated to the SOC scale ($r = 0.27$, $r = 0.68$) and HI ($r = 0.49$, $r = 0.67$).

5.3.2 Reliability

The reliability results showed that Cronbach's alpha values and the ICC coefficients were ≥ 0.70 and ≥ 0.60, respectively. However, when the scores of the PCS and MCS measures were evaluated by paired t-tests, a significant change was noted from T1 to T2. At the same time, the participants' ratings of the eight scales showed no statistical changes, except for the RE and MH scales.

## 5.4 CHANGES IN HRQOL AND COPING ABILITIES (STUDY III)

Changes from baseline to the 6-month follow-up in HRQoL (EORTC QLQ-C30, HI) and the various coping scales scores (SOC, SPS and positive and negative RCOPE) between women with breast cancer and the controls are presented in Figures 3-5. Within the breast cancer group mean differences in global QoL (p < 0.001), all functional scales (p < 0.01), most symptom scales (p < 0.05) (except for dyspnea, insomnia, appetite loss and diarrhoea), the SOC (p < 0.001), SPS (p < 0.001) and positive RCOPE scale (p < 0.001) were statistically significant from T1 to T2. The patients rated worse the functional and symptom scales and lower SOC, SPS and positive RCOPE scale; however, the rated global QoL (p < 0.001) and emotional functioning (p < 0.001) scales were better at T2. In the control group global QoL and most scales remained stable from T1 to T2, except for the role (p < 0.001) and emotional functioning (p < 0.05) scales, two symptom scales, pain (p < 0.01) and diarrhea (p < 0.05), the HI (p < 0.01) and the SOC scale (p < 0.05). In the breast cancer group the effect size changes were >0.80 for the physical and role functioning scales, whereas in the control group the effect size was ≤0.20 in all variables.
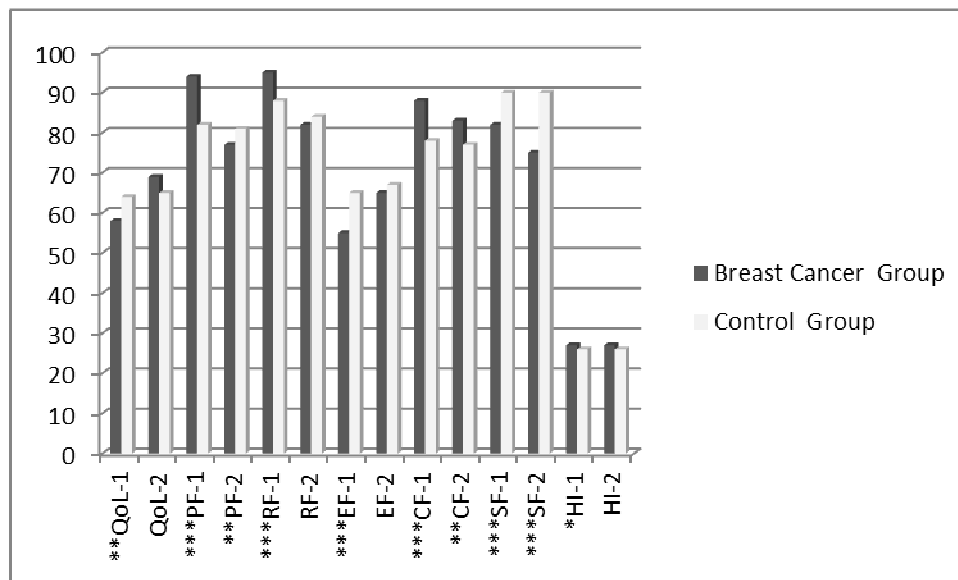
Figure 3. Changes in the functional scales scores of the EORTC QLQ-C30 and the HI in women with breast cancer (n=162) and controls (n=639) at baseline (1) and at the 6-month follow-up (2).
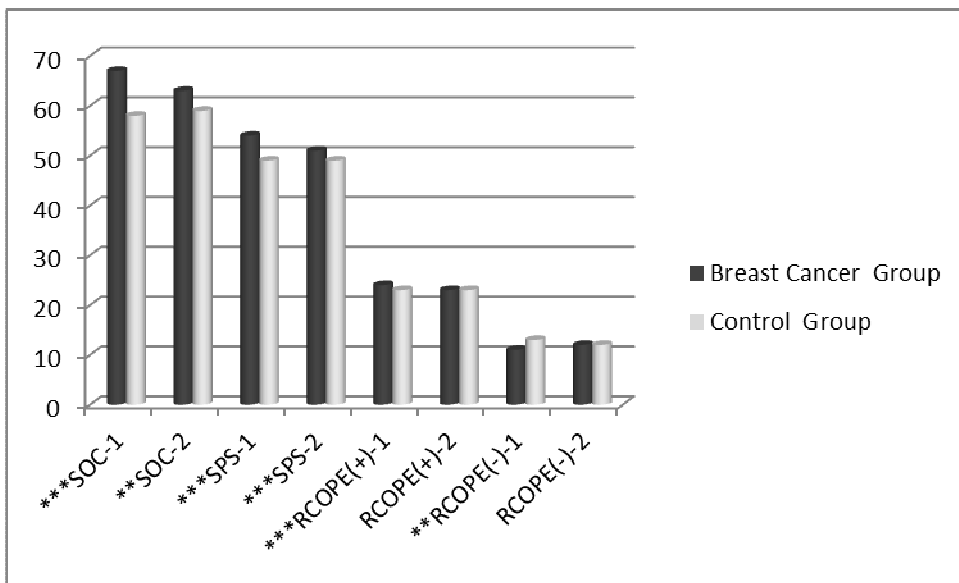The higher the score the better the quality of life, functioning and well-being.
*P < 0.05, **p < 0.01, ***p< 0.001
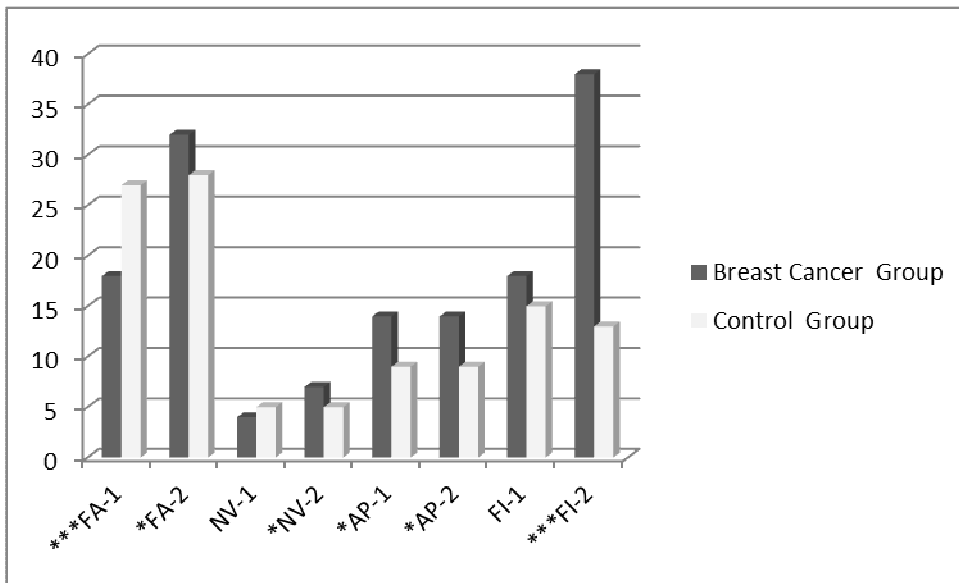
Figure 4. Changes in the significant symptom scales scores of the EORTC QLQ-C30 in women with breast cancer (n=162) and controls (n=639) at baseline (1) and at the 6-month follow-up (2). The higher the score the more reported symptoms.
*P < 0.05, **p < 0.01, ***p< 0.001

Figure 5. Changes in SOC, SPS and RCOPE scales scores in women with breast cancer (n=162) and controls (n=639) at baseline (1) and at the 6-month follow-up (2).
The higher the score the higher SOC, spirituality, use of positive religious coping and more use of negative religious coping.
*P < 0.05, **p < 0.01, ***p < 0.001

The mean differences between the breast cancer and control groups were significant for most outcome variables at T1, where the breast cancer group rated lower scores for the global QoL scale (p < 0.01) and the emotional and social functioning scales (p < 0.001), as well as a higher score for appetite loss (p < 0.05). However, the breast cancer group rated lower scores than the controls in other symptom scales (fatigue, pain, dyspnea, constipation and diarrhea) (p < 0.05) and higher scores (p < 0.001) on the physical, role and cognitive functioning scales. The breast cancer group also showed higher ratings on the HI (p < 0.05), SOC (p < 0.001), positive RCOPE scale (p < 0.001)

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and SPS (p < 0.001), but lower ratings on the negative RCOPE scale (p < 0.01) than the controls at T1. The number of statistically significant differences between the two groups was less at T2. The women with breast cancer reported lower ratings on the physical (p < 0.01) and social functioning (p < 0.001) scales, higher scores for symptoms (fatigue, nausea/vomiting, appetite loss and financial difficulties) (p < 0.05) and higher ratings on the SOC (p < 0.01) and SPS (p < 0.001) scales than the controls. Effect size ≥0.80 between groups at T1 appeared in the physical functioning and SPS scales. At T2, the effect size was ≥ 0.80 for the social functioning scale and financial difficulties. Furthermore, the mean and SD of the SF-12v2 scales (only shown here in the thesis) are summarized in Table 5.

Table 5. Mean differences and clinical changes in the SF-12v2 scales scores (impairment↓ or improvement↑) in women with breast cancer (n = 162) and controls (n = 639) from baseline to the 6-month follow-up.

Variables	Breast cancer group Mean (SD)		P[a] value	Control group Mean (SD)		P[b] value	EF[c]	P[d] value	Change[e]
SF-12v2*	Time (1)	Time (2)		Time (1)	Time (2)				
PF	89.7 (20.6)	68.4 (26.4)	0.000	68.8 (28.5)	69.2 (27.4)	0.728	0.80	0.000	20.9 (↓)
RP	78.8 (24.3)	58.5 (25.3)	0.000	67.9 (23.9)	68.9 (23.1)	0.333	0.80	0.000	19.4 (↓)
BP	88.1 (20.5)	70.8 (26.5)	0.000	72.2 (26.0)	73.5 (26.0)	0.212	0.64	0.000	16.4 (↓)
GH	34.3 (21.1)	53.7 (23.1)	0.000	48.5 (23.1)	49.8 (23.4)	0.126	0.80	0.000	18.1 (↑)
VT	60.8 (24.7)	53.1 (25.0)	0.001	55.3 (24.0)	57.2 (22.8)	0.054	0.24	0.000	5.9 (↓)
SF	79.0 (26.8)	65.6 (30.6)	0.000	70.3 (27.7)	72.6 (27.3)	0.062	0.40	0.000	11.7 (↓)
RE	72.2 (25.5)	65.3 (25.0)	0.002	66.2 (24.9)	67.0 (24.0)	0.402	0.24	0.001	6.3 (↓)
MH	53.2 (19.2)	61.0 (22.4)	0.000	60.5 (23.5)	61.5 (24.3)	0.264	0.30	0.011	5.4 (↑)
PCS	50.9 (6.7)	44.7 (8.9)	0.000	45.6 (8.9)	45.9 (8.7)	0.319	0.70	0.000	5.8 (↓)
MCS	42.6 (10.4)	44.1 (11.5)	0.112	44.4 (11.3)	45.1 (11.2)	0.105	0.07	0.796	0.3 (↑)

* High scores reflect better physical and mental health.
[a] paired Student t-test. [b] paired Student t-test. [c] Effect size between groups, (Criteria: none < 0.20, small 0.20-0.49, moderate 0.50-0.79, large ≥ 0.80). [d] Interaction effect (group by time) by mixed ANOVA adjusted for comorbidity. [e] Differences in changes between groups over time calculated by change in mean score (T2-T1) in the patients with breast cancer minus change in mean score (T2-T1) in the control group.
(Criteria for differences in change; small 5-10, moderate 11-19, large ≥ 20).

The mixed ANOVAs, adjusted for comorbidity, revealed an interaction effect between group (breast cancer group vs. the control group) and time (T1 vs. T2). The breast cancer group, in comparison with the control group, scored significantly lower on the majority of the functional scales (p < 0.01) and reported more symptoms (p < 0.01) (fatigue, nausea/vomiting, pain, constipation and financial difficulties). Further, breast cancer patients scored significantly lower in the HI (p < 0.01), the SOC scale (p < 0.01), the SPS (p < 0.01) and the positive RCOPE scale (p < 0.01), but higher on the global QoL (p < 0.01) and emotional functioning (p < 0.01) scales from T1 to T2. Deterioration in three dimensions (p < 0.001) of the EORTC QLQ-C30 (physical functioning, fatigue and financial difficulties) was regarded as clinically significant.

The means of the scales of the EORTC QLQ-BR23 at the 6-month follow-up in the women with breast cancer were as follows: body image (mean = 68.9, SD = 31.1), sexual function (mean = 80.4, SD = 20.1), sexual enjoyment (mean = 59.9, SD = 19.9),

future perspective (mean = 52.3, SD = 32.1), systemic side effects (mean = 24.4, SD = 18.9), breast symptoms (mean = 17.1, SD = 17.5), arm symptoms (mean = 24.8, SD = 17.8) and upset because of hair loss (mean = 48.0, SD = 37.3). Patients answered all items in the scales of the EORTC QLQ-BR23 (n = 162), except for the two scales sexual enjoyment (n = 74) and upset because of hair loss (n = 59).

5.5 PREDICTORS OF HRQOL AT THE 6- MONTH FOLLOW-UP (STUDY III)

The results showed that the most common predictors of the EORTC QLQ-C30 and HI, 6 months after pre-diagnosis for women with breast cancer were the degree of SOC ($p \leq 0.01$) and baseline ratings ($p \leq 0.01$) in several dimensions of the EORTC QLQ-C30 (e.g., PF, FA, PA, DY, SL, CO and FI) and baseline HI. Whereas the negative RCOPE scale was a predictor of cognitive functioning, body image and future perspective, the SPS and positive RCOPE scale could not predict any of these variables. The results of the regression analyses for predictors of the EORTC QLQ-C30 and HI in the control group after the 6-month follow-up indicated that the SOC scale was the most common predictor ($p < 0.05$) for global QoL, RF, EF, CF, SF, all symptoms (FA and N/V, PA, DY, SL, AP, CO, DI and FI) and HI.

5.6 MEDIATIONAL EFFECT OF THE SOC SCALE (STUDY IV)

Hierarchical multiple regression results from 13 mediational models revealed that at T2 SOC functioned as a mediator ($p < 0.01$) for the rating of the following dimensions of the EORTC QLQ-C30, SF-12v2 and HI from T1 to T2: global QoL, EF, CF and SF, FA and FI from the EORTC QLQ-C30, and GH, MCS, VT, RE, MH, and SF from the SF-12v2, and HI which are summarized in Table 6. A significant mediational effect of SOC-T2 was estimated by the Sobel test, which was significant for all variables, except for FI. Thus, for further confirmation, the bootstrap method was used for all variables and the results revealed a significant effect of SOC-T2 for changes of FI between T1 and T2. Moreover, the results showed that the degree of SOC at T2 completely mediated variation of the global QoL, CF, SF and GH from the EORTC QLQ-C30 and SF-12v2 from T1 to T2. For the remaining variables, the degree of SOC at T2 indicated a partial mediating role (EF, FA, FI, HI, MCS, VT, RE and MH). According to equation three of the regression analyses, the models with the SOC scale as a mediator explained 16% to 45% of the variances in the dependent variables (HRQoL dimensions at T2). Similar pattern was seen when tested the SOC at T1 as mediator (data not shown).

Table 6. Testing the mediational effect of the SOC in relation between HRQoL dimensions at baseline and 6 months later in women with breast cancer (n = 162).

Mediational chain: IV[1] → M[2] → DV[3]	Standardized beta coefficient			Sobel test	Bootstrap			
	IV → M	IV → DV	IV → DV | M[4]		B	SE	CI 95% Lower	CI 95% Upper
EORTC QLQ-C30 Scales:								
1. QoL-T1 → SOC-T2 → QoL-T2	0.27[a]	0.24[b]	0.10	3.26[a]	0.71	0.12	0.45	0.93
2. EF-T1 → SOC-T2 → EF-T2	0.23[b]	0.27[b]	0.16[c]	2.72[b]	0.91	0.12	0.68	1.12
3. CF-T1 → SOC-T2 → CF-T2	0.23[b]	0.16[c]	0.09	2.36[c]	0.41	0.13	0.19	0.65
4. SF-T1 → SOC-T2 → SF-T2	0.18[c]	0.19[c]	0.13	2.04[c]	0.60	0.12	0.36	0.83
5. FA-T1 → SOC-T2 → FA-T2	-0.17[c]	0.25[b]	0.19[b]	2.03[c]	-0.68	0.13	-0.93	-0.42
6. FI-T1 → SOC-T2 → FI-T2	-0.17[c]	0.32[a]	0.29[a]	1.63	-0.52	0.18	-0.88	-0.10
Health Index								
7. HI-T1 → SOC-T2 → HI-T2	0.32[a]	0.48[a]	0.34[a]	3.62[a]	0.14	0.02	0.11	0.18
SF-12v2 Scales:								
8. MCS-T1 → SOC-T2 → MCS-T2	0.37[a]	0.42[a]	0.21[b]	4.36[a]	0.49	0.05	0.37	0.60
9. GH-T1 → SOC-T2 → GH-T2	0.25[a]	0.24[b]	0.14	2.80[b]	0.66	0.13	0.39	0.92
10. VT-T1 → SOC-T2 → VT-T2	0.22[b]	0.36[b]	0.29[a]	2.42[c]	0.62	0.14	0.36	0.90
11. RE-T1 → SOC-T2 → RE-T2	0.33[a]	0.38[a]	0.19[b]	3.98[a]	1.09	0.11	0.87	1.32
12. MH-T1 → SOC-T2 → MH-T2	0.29[a]	0.39[a]	0.23[a]	3.52[a]	0.89	0.11	0.70	1.06
13. SF-T1 → SOC-T2 → SF-T2	0.27[a]	0.22[a]	0.09	3.16[a]	1.11	0.16	0.82	1.43

[a] $p < 0.001$, [b] $p < 0.01$, [c] $p < 0.05$

1. IV, independent variable (HRQoL dimensions at T1)
2. M, mediator,
3. DV, dependent variable (HRQoL dimensions at T2)
4. Relation between IV and DV after controlling for the mediator.

6 DISCUSSION

6.1 PSYCHOMETRIC PROPERTIES OF THE INSTRUMENTS

HRQoL and its determinants in women with breast cancer in Iran as a foundation for nursing care are the focus of this thesis. The main determinants of HRQoL are SOC, spirituality and religious coping; however most of the instruments measuring these aspects of HRQoL did not exist in the Persian language when initiating this thesis. Hence, it was initially important to translate and validate five instruments according to standard guidelines. When questionnaires are going to be adapted to another language, the process of cultural adaptation and generating equivalence is required (Jones et al., 2001; Wild et al., 2005).

The main finding of this thesis implies that women with breast cancer in Iran improve emotionally during the first 6 months from the phase of the suspicion of cancer (pre-diagnose). On the other hand the women decreased in physical function, fatigue and financial situation indicating areas of concern. The women's overall view of life as conceptualized as a sense of coherence seems to be a considerable determinant of HRQoL outcomes. Women with higher sense of coherence evaluated better HRQoL than those with lower indicating the importance of an individual approach in nursing.

6.1.1 The HI, SOC Scale, SPS, and Brief RCOPE Scale

Overall, evidence of validity was obtained for the HI, SOC Scale, SPS and Brief RCOPE scale from 10 posed hypotheses of which six were confirmed. The confirmed hypothesis of a correlation between the SOC scale and the HI has been found in different populations in Western countries (Langius & Lind, 1995; Forsberg, Björvell, & Cedermark, 1996; Cederfjäll et al., 2001; Markström et al., 2002; Sjöström, Langius-Eklöf, & Hjertberg, 2004; Eriksson & Lindström, 2006; Langius-Eklöf, Lidman, & Wredling, 2009) and is now confirmed in Iranian populations. The hypothesized slight positive correlation between the SOC scale and the SPS in study I and III was consistent with earlier assumptions (Strang & Strang, 2001; Gibson & Parker, 2003; Nygren et al., 2005; Delgado, 2007). This finding could indicate that both spirituality and SOC are linked together as an inner strength that mediates successful coping with stressors (Nygren et al., 2005; Strang & Strang, 2001). Concerning the correlation between positive and negative RCOPE scales, a slight positive correlation was found, indicating a distinction between the two scales as proposed by the developer (Pargament et al., 1998). A recent review regarding current psychometric evaluations of the brief RCOPE scale reports that the majority of the studies did not find a significant correlation between positive and negative RCOPE though a few studies did report a positive correlation (Cumming & Pargament, 2010). This was also the pattern in the samples in study III both at baseline and 6 months later. The regression models at baseline and at the 1-month follow-up further strengthened the hypotheses regarding the validity of all four instruments. Although the four exploratory hypotheses were rejected they were very close to the expected and confirmed in the regression models, therefore interpreted to be of minor threat with respect to validity.

The most notable finding was that the SOC scale proved to be a stronger predictor of well-being than religious coping and spirituality (Cohen & Dekel, 2000; Kivimäki et al., 2000; Suominen et al., 2001; Pallant & Lae, 2002; Sjöström, Langius-Eklöf, & Hjertberg, 2004). This finding is congruent with the theory of SOC, which emphasizes

an individual's overall view of life as more important to outcomes of health and well-being than specific coping strategies (Antonovsky, 1987). This finding was further confirmed in study III and IV, whereas SOC went out as a strong predictor and mediator for well-being in the sample of women with breast cancer.

Overall, support for the reliability of the HI, SOC scale, SPS and Brief RCOPE scale was provided by high internal consistency and stability as well as fitted item-total. The internal consistency of these instruments in a sample of women with breast cancer (study III and study IV) and in a control group (study III) was also highly satisfying.

6.1.2 PSYCHOMETRIC PROPERTIES OF THE SF-12V2

The factor structure of the Iranian version of the SF-12v2 with four models was confirmed in a healthy sample. Factorial models, including a two-factor structure (PCS and MCS) and factor loadings were similar to the original version (Ware et al. 1996, 2002), except the models that permitted cross-loadings. In these models general health (GH) was loaded on the mental component rather than the physical component as proposed. It is also reported in a validation study of the Iranian SF-36 (Montazeri et al., 2005). In the original model, it was hypothesized that GH might be cross-loaded to both components (McHorney, Ware, & Raczek, 1993; Ware, 2000). The General Health item (GH) obviously has mixed factor content (Ware, 2000) and the pattern in the respondents' ratings of GH might be a reflection of cultural predisposition in that the same phenomenon appeared in several other Asian countries (Fukuhara, 1998; Tseng, Lu, & Gandek 2003). When the models were compared with each other, the models of two factors and eight subscales with or without cross-loadings showed better model fit than those with two factors and 12 separate scales of each item in this Iranian version. Furthermore, evidence for reliability was acceptable. Therefore, the Iranian version of the SF-12v2 seems to be as reliable and valid instrument as it is in other countries. However, it should be noted that a slight different item loading on the respective component occurred in the present study. This finding, though, does not threaten the use of the instrument as this difference in item loading is accounted for in the model of Ware et al. (1996, 2000).

During the time this thesis was in progress, a parallel study (in Iran) was undertaken regarding translation and psychometric testing of the SF-12 version 1 and 2 (Montazeri, et al. 2009, 2011) in a larger sample size. In this study reliability and validity of the instrument were supported.

6.2   HRQOL THE FIRST 6 MONTHS WITH BREAST CANCER

At the pre-diagnosis stage, the women with breast cancer rated lower global QoL, lower emotional and social functioning and more appetite loss, but better physical, role and cognitive functioning and less fatigue, pain, dyspnea and bowel problems than the controls. However, 6 months later, the women with breast cancer developed more fatigue, financial difficulties, nausea/vomiting and lower physical functioning. Meanwhile, the women with breast cancer still rated social functioning and appetite loss as lower compared with the controls. Before the final diagnosis, the women with breast cancer were not physically affected, but were more emotionally affected than the control women. It could be hypothesized that they were in a more threatening situation because of a suspect tumor (Liao et al., 2008) than the control women who visited mammography for screening on own initiative or on referral. The fact that the

women with breast cancer, despite not yet established, had better ratings on several scales that measured physical features and had less symptoms than the controls could be explained by more comorbidities in the controls.

However, over the 6-month follow-up most changes were statistically significant in the women with breast cancer after controlling for the interaction between time and group and adjusting for comorbidity. Most functional scales and symptoms (fatigue, nausea/vomiting, pain, constipation and financial difficulties) as well as well-being deteriorated in the women with breast cancer, but global QoL and emotional functioning improved. A similar pattern has been reported in an Iranian prospective study without a control group 3 months after initial treatment in a sample of women with breast cancer (Montazeri et al., 2008). Congruent with the findings of this thesis, a Scandinavian study found decreased physical and role and social functioning and increased emotional functioning and fatigue (Brandberg et al., 2003). However, the authors also found a decrease in global QoL. Thus, it seems that most patients recover from the first emotional reactions (Härtl et al., 2010a), although side effects are likely to increase because of treatment (Salonen et al., 2011). However, other studies show slightly different results from our study and the above mentioned studies when looking at the first 6 months after pre-diagnosis. One study with a baseline at the time of established diagnosis and that included a 3-month follow-up found no change in overall QoL, physical functioning, fatigue, nausea/vomiting and financial difficulties in women with breast cancer. However, role, emotional, cognitive and social functioning were found to deteriorate and pain decreased (Schou et al., 2005).

The discrepancies between the studies might depend on several factors, such as type of treatment and its duration, absence of a matched control group and when the follow-ups are actually performed in relation to diagnosis and treatment. The present study and the only study published using EORTC with a pre-diagnosis baseline are both from Iran and have very similar results (Montazeri et al., 2008). This similarity might indicate the importance of a pre-diagnosis rating of HRQoL dimensions in women suspected of having breast cancer. Although there are statistically significant changes, it is always important to determine whether the results have clinical relevance (Fayers & Machine, 2007). Most studies do not take this matter into consideration. The most important clinical relevant changes in the present study appeared in the dimensions of physical functioning, fatigue and financial difficulties. These areas have been recognized previously as being important (Montazeri et al., 2008; Hatam et al., 2011). Physical impairment and fatigue may continue for a long period postoperatively and have been suggested to threaten the patients' independency (Taira et al., 2011). Financial difficulties have been reported in low-, middle- and high-income countries as a dimension affected by having breast cancer (Arndt et al., 2005; Hatam et al., 2011). Financial burden may result from several causes, including work absence, long sick leave, treatment costs and traveling costs to and from the hospital. Presently, treatment costs are not fully covered in Iran (Ibrahimpour et al., 2011).

The results of the SF-12v2 (only presented in the thesis) confirm the findings of the EORTC QLQ-C30. Six months after pre-diagnosis, the women with breast cancer showed deterioration on the physical subscales, except for general health (an index of global QoL), which increased 6 months later.

6.3 PREDICTORS OF HRQOL 6 MONTH AFTER PRE-DIAGNOSIS

Overall, the most important predictors of HRQoL dimensions 6 months after pre-diagnosis of breast cancer were the baseline ratings of each dimension and the degree of SOC. Baseline levels were the most conspicuous predictors of HRQoL, especially regarding general symptoms (fatigue, pain, dyspnea, insomnia, constipation and financial difficulties).

Higher education contributed to explaining increased global QoL and decreased appetite. Interestingly, several HRQoL dimensions related more to stage of the breast cancer than the types of treatment, which is contrary to previous studies (Brandberg et al., 2003; Lee et al., 2011). The patients in the present study that had a severe stage of breast cancer reported a greater degree of impairment in physical functioning, and more diarrhea and systemic side effects. Patients with breast conservation surgery, in comparison to the patients with mastectomy, reported higher emotional functioning and body image and more breast symptoms.

In this thesis the importance of the other measures of coping, religious coping and spirituality to HRQoL dimensions were not as strong as sense of coherence. They showed to be of minor clinical relevance in the patients with breast cancer in comparison to the controls over time. More use of negative religious coping contributed to explain lower cognitive functioning, body image and future perspective, whereas positive religious coping and spirituality did not contribute to the explanation of any of the HRQoL dimensions. It seems that negative religious coping as a less favorable coping strategy in the form of religious struggle is used more by the patients with breast cancer at the 6-month follow-up than positive religious coping and spirituality. These results are consistent with those of a prospective study with a 1-year follow-up on patients with breast cancer (Hebert et al., 2009). This study found associations between negative religious coping and negative HRQoL outcomes (worse mental health, depressive symptoms and lower life satisfaction), whereas positive religious coping were not associated with the HRQoL outcomes. More attention to negative religious coping in Iranian women with breast cancer might be considered as a recognition resource for finding deterioration in dimensions of HRQoL.

6.4 THE ROLE OF SOC AS PREDICTOR

The three major impaired dimensions (physical functioning, fatigue and financial difficulties) were all associated with a lower degree of SOC and worse baseline levels of these three dimensions. Higher SOC with a stress buffering power may contribute to more adaptive abilities in specific situations (Antonovsky, 1987). Meditational tests were performed to determine whether the SOC mediated the role of baseline values of HRQoL to follow-up values of HRQoL. The findings in the context of this thesis indicate that from the pre-diagnosis phase of breast cancer up to 6 months later, SOC worked as a partial or total mediator in the relation between the baseline ratings of HRQoL and the same variables 6 months later, which supports a predictive-protective role of the SOC over time. The partial mediating role of the SOC in the relation to the baseline ratings of emotional function, fatigue, financial difficulties, well-being, mental health, role emotional and vitality may suggest that there are other factors influencing or mediating these relations (e.g., psychological factors, which should be focused on in further research) (Yarcheski, Scoloveno, & Mahon, 1994; Floyd et al., 2010).

One important aspect that is often discussed in the literature is whether SOC is a stable or dynamic predictive-protective factor. Antonovsky (1987) noted that there are probably changes in the level of SOC after exposure to stressful situations. Particularly noteworthy is that the present findings revealed that the degree of SOC was statistically higher in the patients with breast cancer both at baseline and 6 months later, even though it significantly decreased in the women with breast cancer but remained stable in the control group over time. However, the effect size indicated that the differences were of little clinical relevance (a change of a score more than 10 points or calculation of effect size). There is lack of normative data for SOC scores in the Iranian population, but in comparison with the healthy sample in study I collected in the same region and a sample of family caregivers of the patients included in this thesis (Khanjari, Oskouie, & Langius-Eklöf, 2011), the women with breast cancer gave a much higher SOC rating at baseline and 6 months later than all the other samples. One explanation to account for this finding could be that women in the control group had more comorbidity probably also related to a lower socioeconomic level and lower SOC (Kivimäki et al., 2000; Smith, Breslin, & Beaton, 2003; Ing & Reutter, 2003).

Some studies have questioned the stability of the SOC scale (Nilsson et al., 2003; Feldt et al., 2003), whereas other studies have confirmed its stability (Feldt et al., 2000, Langius-Eklöf & Samuelsson, 2009). Antonovsky and others suggest that variations over time are small (Antonovsky, 1987; Lindström & Eriksson, 2005). In the present study the degree of SOC decreased significantly during the illness trajectory between the pre-diagnose phase and 6 months later; however, this finding was not clinically relevant. This might be concluded that a diagnosis and the following distress might influence the individual's overall life orientation, i.e. that life is now less comprehensible, manageable and meaningful. The mediating role of the SOC and its closer relation to the psychological dimensions of HRQoL suggest a stronger relation between SOC and mental health than between SOC and physical health, which would be consistent with previous studies (Eriksson & Lindström, 2006; Ying & Lee, 2007; Wiesmann, Niehörster, & Hannich, 2009; Ying, 2009). This issue poses the question of whether the concepts of SOC and mental health are equivalent. Previous findings indicate that SOC and mental health are correlated concepts, but distinct (Langius-Eklöf & Samuelsson, 2009; Drageset & Lindstrom, 2008; Eriksson & Lindström, 2006), implying that a high SOC does not indicate the absence of anxiety and depression but more likely the capacity to cope with life's stressors. SOC may be regarded as a crucial element in the structure of an individual's personality that contributes to psychological functioning in a recovery process (Grifiiths, 2009).

The impairments in HRQoL and the experience of psychological distress should be considered as conditions influenced by different factors. Boscaglia and Clarke (2007) described psychological distress as a syndrome, suggesting that higher SOC can be protective against psychological distress. However, the authors noted that there could be additional variables that require examination for further clarification. To explain the underlying mechanism of the protective role of the SOC, according to Antonovsky's (1987) theory, SOC is a trait that reflects the personal power to respond to life events and challenging situations. Therefore, a strong SOC as an inner resource can influence the patients' recovery and provide the possibility to enhance it by applying health behaviors (Nygren et al., 2005; Lundman et al., 2010).

In this thesis the influence of the degree of SOC was more pronounced than religious coping and spirituality, which is contrary to several studies showing the power of religion and spirituality on health and well-being in a Muslim context (Rezaei et al., 2008; Taleghani et al., 2006, 2008; Harandi, 2010). The present results do not diminish the importance of religious coping and spirituality, but rather underscore that the overall view of life might be more important than a particular relationship to God. Thus, a dispositional orientation captures the character traits (Antonovsky, 1987, 1993).

6.5 METHODOLOGICAL CONSIDERATIONS

Five well-known standardized self-reported instruments were selected and carefully translated and culturally adapted. HRQoL is a multidimensional concept (Bottomly, 2002) and therefore it is impractical to assess all the dimensions of HRQoL simultaneously in one instrument. Thus, to cover different aspects of HRQoL multiple instruments should be applied (Fayers & Machine, 2007). Using multiple instruments was of no concern for the present thesis as the dropout rates were acceptable. The major strengths of the study are the use of baseline measures before final diagnosis and 6-month follow-up and the use of a control group.

In our study Cronbach's alpha coefficients were below the suggested level in some of the scales/items in the EORTC QLQ-C30 (role and cognitive functioning and nausea/vomiting) and in the EORTC QLQ-BR23 (arm symptoms), though consistent with previous findings (Montazeri et al., 1999, 2000; Schou et al., 2005; Awad, Denic, & EI Taji, 2008). The low coefficients for these items could be due to the low number of items on these scales (Nunnally & Bernstein, 1994). However, all scales/items of the EORTC QLQ-C30 met the criteria at the 6-month follow-up.

One limitation is the sample in study I and II. The sample was a non-random selection of people who were healthy and rather well-educated. Thus, the sample was to some extent not a representative sample of the Iranian population, which means the results cannot be generalized, even though the power analysis showed the sample size reasonable.

The women with breast cancer were selected consecutively and therefore are probably representative of the setting. However, because no data were collected for those declining participation, the findings might be biased. The participants in the control group were randomly selected during odd and even days per week. There is no reason to suspect that randomization did influence on variation of extraneous variables in sampling (Polit & Beck, 2008).

Another limitation is that chemotherapy and not the specific types were registered. If this had been done more precisely, more definitive conclusions could have been drawn.

A further limitation of the study is the differences between the patients with breast cancer and the controls. The groups were expected to be similar but there was more co-morbidity in the control group. The reason for this may be that the women already in hospital care for a suspect lump are not representative of the population of women who sought or were referred to mammography. The best option would have been to study all women in a screening program and follow both those diagnosed with breast cancer and those not diagnosed with breast cancer. However, this option was not possible because Iran does not have such a screening program. This difference comorbidity was

controlled for in the statistical tests. Another potential bias in this study is that co-morbidity was obtained from medical records in the breast cancer group but by self-reports in the control group. Still, it should be noted that subjective reports of comorbidity could bring greater variation of the results in comparison with a validated record-based system (Voaklander et al., 2004). Thus, generalization of the results should be done cautiously.

7 NURSING IMPLICATIONS

It is important to implement nursing interventions in patients with suspect breast cancer early at the first visit and continue throughout treatment and the follow-up period. The assessment of HRQoL and SOC could serve as a foundation for the interventions. Instruments of HRQoL might measure aspects of ill-health rather than health (Bringsen et al., 2009) and the salutogenic feature still might remain. Health and quality of life are core concepts in nursing (Plummer & Molzan, 2009). Health from a salutogenic and nursing perspective concerns promoting and remaining healthy rather than curing diseases (King, 1994). The nursing perspective refers to the patient perspective as also taking in account by using self-administrated questionnaires and not proxy measures or assessment (Fayers & Hays, 2005). Questionnaires might be controversial in in relation to discussions about the patients' life world. However, it is important to have a holistic perspective when using the patients' ratings and discuss the results in relation to the individual patient's life world (King et al., 2002; King, 2006).

The major findings of this thesis indicate that women with breast cancer need individualized care. However, special attention should be given to physical functioning, fatigue and financial difficulties. To develop a broad supportive, recovery and interventional plan, including the possibility to counseling, psychosocial support and exercise training (Herrero et al., 2006; Goodwin et al., 2007). The importance of coping needs should be considered in nursing care in relation to interventions. Nurses should consider the concept of SOC as a potential pathway for finding the meaning in a patient's life and contribute to the patient's successful coping with the cancer trajectory. Nursing assessment can consist of the assessment of HRQoL, but this should be immediately followed with discussions of the outcome with the patient in relation to how the patient found the situation comprehensible, manageable and meaningful. Even though it is not probably possible to increase a patient's sense of coherence, nursing care should strive to make each situation comprehensible, manageable and meaningful for each patient.

8 CONCLUSIONS

The SOC, HI, SPS, RCOPE and SF-12v2 were found to be psychometrically sound instruments, for use in Iran.

Overall, in this sample of women with breast cancer in Iran with a baseline before diagnosis and in comparison to a control group, physical functioning, fatigue and financial difficulties were prominent areas of impairment in the dimensions of HRQoL during the first 6 months after pre-diagnosis of breast cancer. At the same time, patients with breast cancer improved in their perception of global quality of life and emotional functioning.

The concept of SOC seemed to be a stronger predictor and mediator than religious coping and spirituality in explaining changes in HRQoL dimensions and well-being in this sample of women with breast cancer. The relation between HRQoL dimensions and SOC indicates how the degree of SOC may be embedded in the recovery process of patients with breast cancer. Sense of coherence might function as a predictive-protective mediator for HRQoL dimensions in the process of psychological adaptation with a cancer trajectory.

Additional to the degree of sense of coherence, baseline ratings of the respective dimensions in health-related quality of life were important predictors of ratings at the 6-month follow-up.

The present results direct attention to the need to focus on evaluation of HRQoL outcomes together with SOC in breast cancer patients within an integrated care plan already at the time of diagnosis.

9 FUTURE RESEARCH

Further studies will benefit from longer follow-ups and using matched controls. Further testing with SOC as a mediator is recommended using longitudinal designs. Moreover, religious coping and spirituality in women with breast cancer need to be studied under the above conditions.

The thesis focused on dimensions of HRQoL using standardized self-reported instruments. In the future qualitative studies that encompass the individual perspective out from the life world will contribute the goal of obtaining more knowledge about the meaning of health related quality of life and lived experience of having a breast cancer.

10 ACKNOWLEDGEMENTS

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